

# Penalized Variable Selection for Multi-center Competing Risks Data

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## Abstract

We consider variable selection in competing risks regression for multi-center data. Our research is motivated by deceased donor kidney transplants, from which recipients would experience graft failure, death with functioning graft (DWFG), or graft survival. The occurrence of DWFG precludes graft failure from happening and therefore is a competing risk. Data within a transplant center may be correlated due to a latent center effect, such as varying patient populations, surgical techniques, and patient management. The proportional subdistribution hazard (PSH) model has been frequently used in the regression analysis of competing risks data. Two of its extensions, the stratified and the marginal PSH models, can be applied to multi-center data to account for the center effect. In this paper, we propose penalization strategies for the two models, primarily to select important variables and estimate their effects whereas correlations within centers serve as a nuisance. Simulations demonstrate good performance and computational efficiency for the proposed methods. It is further assessed using an analysis of data from the United Network of Organ Sharing.

## 1 Introduction

Kidney transplant is the most cost-effective therapy for patients with end-stage renal disease, prolonging survival and improving quality of life. This practice is undergoing a tremendous shortage of organs. As of September, 2015, over 100,000 patients are on the waiting list in the United States (OPTN/SRTR, 2011). From 2004 to 2014, the annual number of kidney transplants barely changed, ranging from 16,000 to 17,000 (OPTN/SRTR, 2011), which is greatly disproportionate to the demand. Expanded donor criteria kidneys from older and sicker donors are being procured as a reaction to the shortage, which has led to greater discard rates of donated kidneys as well as

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more complications for recipients, including shorter graft survival (Port et al., 2002). Proper allocation of kidneys is more important than ever.

The Organ Procurement and Transplantation Network (OPTN) approved a new national deceased donor kidney allocation policy in 2013 in reaction to this shortage, which prioritizes candidates with longer estimated life expectancy to receive kidneys with the potential to function longer. The Kidney Donor Risk Index (KDRI) (Rao et al., 2009) was adopted to measure graft survival of deceased donor kidneys. Graft survival is defined as the time from the day of transplantation to the earliest onset of graft failure or death. A lower KDRI is associated with longer graft survival. This index includes 10 donor factors, which are identified by a variable selection procedure that sequentially eliminates insignificant factors.

Two complications are present when the primary interest is to specifically predict the risk of graft failure, as opposed to the composite risk of graft failure and death as in the KDRI, using multi-center data. One is the presence of competing risks. After kidney transplantations, recipients may experience graft survival, graft failure, or death with functioning graft (DWFG). Those who have died with a functioning graft can no longer develop graft failure. DWFG is therefore a competing risk to graft failure. The other complication is the center effect arising from available data of deceased donor kidney transplants. The data were collected by an ongoing organ transplant registry of the United Network of Organ Sharing (UNOS) from all transplant centers in the US. Patients within a center may have correlated outcomes due to a latent center effect, such as surgical techniques, patient management, and patient characteristics (Evans et al., 1991; Kim et al., 2004; Taylor et al., 1985). We therefore propose penalized variable selection strategies that account for the presence of competing risks and the center effect. Selected factors can be used to construct prognostic models for predicting the risk of graft failure.

In competing risks regression, the proportional subdistribution hazard (PSH) model (Fine and Gray, 1999) has become popular for its direct assessment of covariate effects on the cumulative incidence function. Some of its extensions can account for within-center correlations. Katsahian et al. (2006) and Christian et al. (2015) proposed a PSH frailty model treating the center effect as a random sample from a distribution. Ha et al. (2014a) extended this model to handle potential heterogeneity in the treatment effect among centers. Zhou et al. (2011) developed a stratified approach to account for varying patient populations by assuming an unspecified center-specific baseline subdistribution hazard. Zhou et al. (2012) proposed a marginal PSH model to estimate effects of covariates on the marginal cumulative incidence function under a working independence assumption; the variance estimator was adjusted to accommodate the within-center correlations.

Several variable selection methods have been extended to the competing risks setting. Kuk and Varadhan (2013) extended stepwise selection to the PSH model, by developing selection criteria based on Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC) and a modified BIC for competing risks data (BICcr). Although simple and easy to use, stepwise selection is computationally intensive and unstable, and its theoretical properties are largely unknown (Fan and Li, 2001; Fu et al., 2015). Fu et al. (2015) developed a generalized penalized variable selection method-

ology for the PSH model and established the asymptotic properties for the penalized estimator. However, the stepwise selection and the penalized PSH model cannot account for the center effect. Ha et al. (2014b) proposed a variable selection procedure that penalizes a hierarchical likelihood of the PSH frailty model. Their method assumes frailties follow a log-normal distribution and simultaneously perform variable selection and estimation of covariate effects and frailties. Efficiency in standard errors is gained if the distribution of frailties is approximately true (O’Quigley and Stare, 2002), but potentially misleading if misspecified. If the study interest only lies in variable selection and estimation of covariate effects, introducing parameters to explicitly model center effects either through indicator variables or frailties does not seem to be worthwhile, because it complicates the analysis of covariates effects and may be subject to numerical difficulties or bias under violations of model assumptions.

In this paper, we propose to extend the penalized variable selection method (Fu et al., 2015) to the stratified and the marginal PSH models, treating within-center correlations as a nuisance. The method for the stratified PSH model can be applied to data exhibiting two types of stratification regimes: the regularly stratified and the highly stratified. The former has a small number of large centers and the latter has a large number of small centers. Center effects are modeled through center-specific subdistribution hazards. The method for the marginal PSH model is suitable for data with a large number of centers. The proposed variance estimator accommodates the correlation within centers. We also briefly describe the extension of the proposed methods to group variable selection, which can select pre-specified groups of variables collectively.

The remainder of this paper is organized as follows. In Section 2, we present the proposed penalization methods and address implementation issues. In Section 3, simulations are conducted to evaluate the performance of the proposed methods. Section 4 applies the methods to the data from the UNOS. Section 5 contains discussion.

## 2 Penalized Variable Selection for Multi-center Competing Risks Data

### 2.1 Notation

Suppose there are  $K$  centers with  $n_k$  patients for center  $k$ ,  $k = 1, \dots, K$ . The total number of observations is  $\sum_{k=1}^K n_k = n$ . Cause 1 of failure is graft failure and cause 2 is the competing risk, DWFG. For patient  $i$  within center  $k$ , denote the failure time, the censoring time, and the failure cause as  $T_{ki}$ ,  $C_{ki}$ , and  $\epsilon_{ki} \in \{1, 2\}$ . Let  $\mathbf{Z}_{ki} = \{Z_{1ki}, \dots, Z_{dki}\}$  be a  $d \times 1$  vector of covariates. We observe  $\{X_{ki}, \delta_{ki}, \delta_{ki}\epsilon_{ki}, \mathbf{Z}_{ki}, \xi_{ki}\}$ , where  $X_{ki} = \min(T_{ki}, C_{ki})$ ,  $\delta_{ki} = I(T_{ki} \leq C_{ki})$  is the event indicator, and  $\xi_{ki} \in \{1, \dots, K\}$  is a center indicator.

Let  $\mathbf{T}_k$  be a vector of  $(T_{k1}, \dots, T_{kn_k})^T$ , and  $\boldsymbol{\epsilon}_k$ ,  $\mathbf{C}_k$ , and  $\mathbf{Z}_k$  are defined similarly. We assume that  $(\mathbf{T}_k, \boldsymbol{\epsilon}_k, \mathbf{C}_k, \mathbf{Z}_k)$  are independent and identically distributed;  $(\mathbf{T}_k, \boldsymbol{\epsilon}_k)$  and  $\mathbf{C}_k$  are independent given  $\mathbf{Z}_k$ . Patients within center  $k$  are assumed to be exposed to a common center effect, which implies components of  $(\mathbf{T}_k, \boldsymbol{\epsilon}_k)$  may be correlated

conditional on  $\mathbf{Z}_k$ .

## 2.2 Penalized Stratified PSH Model

### 2.2.1 Model

The stratified PSH model (Zhou et al., 2011) is a conditional (or center-specific) approach that models the subdistribution hazards for graft failure in each center separately. It can be regarded as an analogy of the stratified Cox model for the competing risks setting. For center  $k$ , the cumulative incidence function for graft failure is defined as  $F_{1k}(t; \mathbf{Z}_{ki}) = Pr(T_{ki} \leq t, \epsilon_{ki} = 1 | \mathbf{Z}_{ki}, \xi_{ki} = k)$ . The corresponding subdistribution hazard is  $\lambda_{1k}(t; \mathbf{Z}_{ki}) = dF_{1k}(t; \mathbf{Z}_{ki}) / \{1 - F_{1k}(t; \mathbf{Z}_{ki})\}$ . Assuming proportional subdistributional hazards,  $\lambda_{1k}(t; \mathbf{Z}_{ki})$  can be written as

$$\lambda_{1k}(t; \mathbf{Z}_{ki}) = \lambda_{1k0}(t) \exp(\boldsymbol{\beta}^T \mathbf{Z}_{ki}), \quad (1)$$

where  $\lambda_{1k0}(t)$  is an unspecified center-specific baseline subdistribution hazard, and  $\boldsymbol{\beta}$  is a  $d \times 1$  vector of regression coefficients. Within-center correlation arises from all patients being exposed to a common center effect.

The log-partial likelihood function is a linear combination of the likelihood for every center and is defined as

$$\begin{aligned} l^S(\boldsymbol{\beta}) &= \sum_{k=1}^K l_k(\boldsymbol{\beta}) \\ &= \sum_{k=1}^K \sum_{i=1}^{n_k} \delta_{ki} I(\epsilon_{ki} = 1) \{ \boldsymbol{\beta}^T \mathbf{Z}_{ki} - \log \sum_{i'=1}^{n_k} \hat{w}_{ki'}(X_{ki}) Y_{ki'}(X_{ki}) \exp(\boldsymbol{\beta}^T \mathbf{Z}_{ki'}) \}, \end{aligned} \quad (2)$$

where  $l_k(\boldsymbol{\beta})$  is the log-partial likelihood for center  $k$ ,  $Y_{ki}(t) = 1 - I(T_{ki} \leq t-, \epsilon_{ki} = 1)$  indicates whether the patient is still at risk of graft failure, and  $\hat{w}_{ki}(t)$  is a time-dependent weight for patient  $i$  within center  $k$ . Under the two stratification regimes,  $\hat{w}_{ki}(t)$  is defined differently using the inverse probability of censoring weighting techniques (Robins and Rotnitzky, 1992; Zhou et al., 2011) to achieve unbiased estimation. For regularly stratified data, observations are assumed to be i.i.d. within centers and the censoring distribution is center-dependent. In this case, the weight is defined as  $\hat{w}_{ki}(t) = I(C_{ki} \geq T_{ki} \wedge t) \hat{G}_k(t) / \hat{G}_k(X_{ki} \wedge t)$ , where  $G_k(t) = Pr(C_{ki} \geq t)$ ,  $i = 1, \dots, n_k$ , and  $\hat{G}_k(\cdot)$  is the Kaplan-Meier estimator of  $G_k(\cdot)$ . It is possible to estimate  $G_k(\cdot)$  from a Cox model by including some potentially important covariates on the censoring. For highly stratified data, observations and censoring are assumed to be i.i.d. across centers, leading to a weight of  $\hat{w}_{ki}(t) = I(C_{ki} \geq T_{ki} \wedge t) \hat{G}(t) / \hat{G}(X_{ki} \wedge t)$ , where  $G(t) = Pr(C_{ki} \geq t)$  is the common censoring distribution,  $i = 1, \dots, n_k$ ,  $k = 1, \dots, K$ . By time  $t$ , if a patient has not experienced any event,  $\hat{w}_{ki}(t) Y_{ki}(t) = 1$ ; if the patient is right censored or has experienced graft failure,  $\hat{w}_{ki}(t) Y_{ki}(t) = 0$ ; if the patient has experienced DWFG,  $\hat{w}_{ki}(t) Y_{ki}(t) = \hat{G}_k(t) / \hat{G}_k(X_{ki})$  or  $\hat{G}(t) / \hat{G}(X_{ki})$  ranging from 0 to 1. Covariate effects are estimated through maximizing function (2) and relative risks obtained from the covariates compare two patients within the same center (Glidden and Vittinghoff, 2004).

To perform variable selection and parameter estimation simultaneously, we use a penalized partial likelihood for the model in equation (1), which is defined as

$$Q^S(\boldsymbol{\beta}) = \sum_{k=1}^K \{l_k(\boldsymbol{\beta}) - n_k \sum_{j=1}^d p_\lambda(|\beta_j|)\} = l^S(\boldsymbol{\beta}) - n \sum_{j=1}^d p_\lambda(|\beta_j|), \quad (3)$$

where  $p_\lambda(|\beta_j|)$  is a penalty function with tuning parameter  $\lambda$ , controlling the complexity of selected models. A larger  $\lambda$  tends to choose a simpler model with fewer selected variables. Function (3) is essentially penalizing the log-partial likelihood of the ordinary PSH model for every center, and the center-specific penalty is  $n_k \sum_{j=1}^d p_\lambda(|\beta_j|)$ . The penalized estimator, denoted as  $\tilde{\boldsymbol{\beta}}^S$ , is the maximizer of the objective function (3),

$$\tilde{\boldsymbol{\beta}}^S = \arg \max Q^S(\boldsymbol{\beta}).$$

Since the proportional hazard specification is conditional on centers,  $\lambda_{1k0}(t)$  has “summed out” in  $l_k(\boldsymbol{\beta})$ . The objective function  $Q^S(\boldsymbol{\beta})$  does not contain the center-specific baseline subdistribution hazards, which incorporate the center effect. Thus, the estimation of  $\tilde{\boldsymbol{\beta}}^S$  is not changed by the center effect.

Various penalty functions have been proposed in other settings; see Fan and Lv (2010) for an extensive review. We consider four popular penalties in this paper, but our results can be extended to other penalties:

- (a). Least Absolute Shrinkage and Selection Operator (LASSO) (Tibshirani, 1996):  $p_\lambda(|\beta_j|) = \lambda|\beta_j|$ .
- (b). Adaptive LASSO (ALASSO) (Zou, 2006):  $p_\lambda(|\beta_j|) = \lambda\theta_j|\beta_j|$ , where  $\theta_j$  is a data-adaptive weight assigned to  $\beta_j$ . We use  $\theta_j = |\hat{\boldsymbol{\beta}}_j^S|^{-1}$ , where  $\hat{\boldsymbol{\beta}}^S$  is the maximizer of the log-partial likelihood function.
- (c). Smoothly Clipped Absolute Deviation (SCAD) (Fan and Li, 2001):  $p'_\lambda(|\beta_j|, \alpha) = \lambda I(|\beta_j| \leq \lambda) + \frac{(\alpha\lambda - |\beta_j|)_+}{(\alpha-1)} I(|\beta_j| > \lambda)$  and  $\alpha > 2$  is a tuning parameter and  $(x)_+$  indicates the positive part of  $x$ .
- (d). Minimax Concave Penalty (MCP) (Zhang, 2010):  $p'_\lambda(|\beta_j|, \gamma) = (\lambda - \frac{|\beta_j|}{\gamma})_+$  and  $\gamma > 1$  is a tuning parameter.

For the ordinary PSH model, Fu et al. (2015) showed the large sample properties of ALASSO, SCAD, and MCP, including selection consistency and the oracle properties, namely, properties of an ideal selection procedure that can work as well as the underlying model were known in advance (Fan and Li, 2001). When stratification is added, we can also demonstrate the consistency and the oracle properties of the three penalties under both stratification regimes: when data are regularly stratified, the number of center is finite and the center size goes to infinity; when data are highly stratified, the number of centers goes to infinity whereas the center size holds finite. Theorems stating the large sample properties of  $\tilde{\boldsymbol{\beta}}^S$  and proofs are included in Appendix A.

### 2.2.2 Implementation Issues

The coordinate descent (CD) algorithm (Friedman et al., 2010; Simon et al., 2011) and the local quadratic approximation (LQA) algorithm (Fan and Li, 2001, 2002) are two implementation methods for penalization methods with convex or non-convex penalties. The former has gained more popularity than the latter for its computational efficiency (Fan and Lv, 2010). To penalize the stratified PSH model, we use the LQA algorithm because the CD algorithm may not perform well when the center size is small.

Two complications arise when applying the CD algorithm to the penalized stratified PSH model with small sizes of centers. First, one step in the CD algorithm is to approximate the objective function by a penalized least square and the optimization problem becomes minimizing  $Q^S(\boldsymbol{\beta}) \approx n^{-1} \sum_{k=1}^K (\mathbf{y}_k - \boldsymbol{\eta}_k)^T (-\partial^2 l_k / \partial \boldsymbol{\eta}_k \partial \boldsymbol{\eta}_k^T) (\mathbf{y}_k - \boldsymbol{\eta}_k) + \sum_{j=1}^d p_\lambda(|\beta_j|)$ , where  $\boldsymbol{\eta}_k = \mathbf{Z}_k \boldsymbol{\beta}$ ,  $\mathbf{Z}_k$  is the design matrix for stratum  $k$  and  $\mathbf{y}_k = \boldsymbol{\eta}_k - (\partial^2 l_k / \partial \boldsymbol{\eta}_k \partial \boldsymbol{\eta}_k^T)^{-1} (\partial l_k / \partial \boldsymbol{\eta}_k)$ . When the center size is small, the event of interest within a center is often rare. Inverting the  $n_k \times n_k$  matrix  $\partial^2 l_k / \partial \boldsymbol{\eta}_k \partial \boldsymbol{\eta}_k^T$  may not be computationally feasible, resulting in the failure of the CD algorithm. For example, three patients in center  $k$  have graft failure, DWFG, and loss to follow-up sequentially, then  $\partial^2 l_k / \partial \boldsymbol{\eta}_k \partial \boldsymbol{\eta}_k^T$  is not positive definite, thus can not be inverted. Second, when the inversion is possible, to reduce computational burden, a conventional method in the CD algorithm is to replace the off-diagonal entries of  $\partial^2 l_k / \partial \boldsymbol{\eta}_k \partial \boldsymbol{\eta}_k^T$  by zeros (Tibshirani, 1996). The replacement works when  $n_k$  is large, because the off-diagonals are much smaller than the diagonals (Hastie and Tibshirani, 1999). When  $n_k$  is moderate to small, the inverted matrix may not be accurate, potentially leading to incorrect selection results.

To implement the LQA procedure, we follow Fan and Li (2001, 2002) to locally approximate the penalty by a quadratic function. Given an initial value  $\boldsymbol{\beta}^{(0)}$  that is close to  $\tilde{\boldsymbol{\beta}}^S$ , the penalty function  $p_\lambda(|\beta_j|)$  is quadratically approximated by

$$p_\lambda(|\beta_j|) \approx p_\lambda(|\beta_j^{(0)}|) + \frac{1}{2} \{p'_\lambda(|\beta_j^{(0)}|) / |\beta_j^{(0)}|\} \{\beta_j^2 - (\beta_j^{(0)})^2\}.$$

Define the score function  $U^S(\boldsymbol{\beta}) = \partial l^S(\boldsymbol{\beta}) / \partial \boldsymbol{\beta}$  and the Hessian matrix  $H^S(\boldsymbol{\beta}) = \partial^2 l^S(\boldsymbol{\beta}) / \partial \boldsymbol{\beta} \partial \boldsymbol{\beta}^T$ . We then apply the Newton-Raphson algorithm to maximize the objective function (3). At iteration  $k + 1$ , the solution is updated by

$$\boldsymbol{\beta}^{(k+1)} = \boldsymbol{\beta}^{(k)} - \{H^S(\boldsymbol{\beta}^{(k)}) - nA_\lambda(\boldsymbol{\beta}^{(k)})\}^{-1} \{U^S(\boldsymbol{\beta}^{(k)}) - n\boldsymbol{\beta}^{(k)} A_\lambda(\boldsymbol{\beta}^{(k)})\}, \quad (4)$$

where  $A_\lambda(\boldsymbol{\beta})$  is a diagonal matrix with entires  $A_j = \frac{p'_\lambda(|\beta_j|)}{|\beta_j|}$ ,  $j = 1, \dots, d$ . To avoid numerical difficulties when  $\beta_j = 0$ , we take the strategy from Hunter and Li (2005) and employ  $A_{j,\epsilon} = \frac{p'_\lambda(|\beta_j|)}{|\beta_j| + \epsilon}$ , where  $\epsilon$  is a small positive value such as  $10^{-6}$ . From equation (4), standard errors for non-zero penalized estimators can be directly obtained using the sandwich formula,

$$\text{cov}(\tilde{\boldsymbol{\beta}}_1^S) = \{H^S(\tilde{\boldsymbol{\beta}}_1^S) - nA_\lambda(\tilde{\boldsymbol{\beta}}_1^S)\}^{-1} \text{cov}\{U^S(\tilde{\boldsymbol{\beta}}_1^S)\} \{H^S(\tilde{\boldsymbol{\beta}}_1^S) - nA_\lambda(\tilde{\boldsymbol{\beta}}_1^S)\}^{-1}.$$

The explicit formula of  $\text{cov}\{U^S(\tilde{\beta}_1^S)\}$  can be found in Zhou et al. (2011).

We employ the Bayesian Information Criteria (BIC) as in Wang et al. (2007) to select tuning parameters:  $\text{BIC}(\lambda) = -2l^S(\tilde{\beta}^S) + \log(n)\text{DF}_\lambda$ , where  $\text{DF}_\lambda$  is the effective number of parameters and can be computed by  $\text{tr}[\{H^S(\tilde{\beta}^S) - nA_\lambda(\tilde{\beta}^S)\}^{-1}H^S(\tilde{\beta}^S)]$ . The optimum  $\lambda$  minimizes  $\text{BIC}(\lambda)$ . For SCAD and MCP, we also need to select values of  $\alpha$  and  $\gamma$ . A two-dimensional grid search is usually conducted to find the best pair of  $(\lambda, \alpha)$  or  $(\lambda, \gamma)$ , but computation can be extensive. Fan and Li (2001) suggested to fix  $\alpha \approx 3.7$  for SCAD from a Bayesian statistical point of view. Zhang (2010) suggested to fix  $\gamma \approx 2.7$  for MCP. For simplicity, we use their suggested values throughout this paper.

### 2.3 Penalized Marginal PSH Model

Different from the penalization strategy in Section (2.2), which identifies important variables for the cumulative incidence function of graft failure conditional on transplant centers, the primary interest of the penalized marginal PSH model is the marginal cumulative incidence function. The standard error of regression coefficients is then corrected for within-center correlations. The marginal cumulative incidence function is defined as  $F_1(t; \mathbf{Z}_{ki}) = P(T_{ki} \leq t, \epsilon_{ki} = 1 | \mathbf{Z}_{ki})$ ,  $i = 1, \dots, n_k, k = 1, \dots, K$ , and the marginal subdistribution hazard can be defined accordingly:  $u_1(t; \mathbf{Z}_{ki}) = dF_1(t; \mathbf{Z}_{ki}) / \{1 - F_1(t; \mathbf{Z}_{ki})\}$ . Zhou et al. (2012) proposed to model  $u_1(t; \mathbf{Z}_{ki})$  with the proportional hazard specification,  $u_1(t; \mathbf{Z}_{ki}) = u_{10}(t) \exp(\beta^T \mathbf{Z}_{ki})$ , where  $u_{10}(t)$  is an unspecified baseline shared by all centers and  $\beta$  has a population-average interpretation. Relative risk of a factor compares two patients who are randomly selected from the population (Wei et al., 1989). The marginal PSH model can be regarded as an analogy of the marginal Cox model proposed by Lee et al. (1992) for the competing risks setting, and it is suitable when the scientific interest is on the study population.

Maximizing the marginal partial likelihood is usually prohibitive in terms of computation. Zhou et al. (2012) proposed a pseudo-partial likelihood function as an alternative to the full likelihood by assuming that event times of graft failure are independent of each other even if they belong to the same center. The log-pseudo-partial likelihood function is defined as follows

$$l^M(\beta) = \sum_{k=1}^K \sum_{i=1}^{n_k} \delta_{ki} I(\epsilon_{ki} = 1) \{ \beta^T \mathbf{Z}_{ki} - \log \sum_{k'=1}^K \sum_{i'=1}^{n_k} \hat{w}_{k'i'}(X_{k'i'}) Y_{k'i'}(X_{k'i'}) \exp(\beta^T \mathbf{Z}_{k'i'}) \}, \quad (5)$$

where  $\hat{w}_{ki}(t)$  is a marginal inverse probability of censoring weight and is defined as  $\hat{w}_{ki}(t) = I(C_{ki} \geq T_{ki} \wedge t) \hat{G}(t) / \hat{G}(X_{ki} \wedge t)$ ,  $i = 1, \dots, n_k, k = 1, \dots, K$ . Note the formulation of the log-pseudo-partial likelihood function is the same as the log-partial likelihood for the ordinary PSH model. Maximizing this likelihood function is computationally advantageous and the estimated regression coefficients are consistent and asymptotically normal (Zhou et al., 2012). Denote the maximizer of function (5)

as  $\hat{\beta}^M$ . The variance estimator of  $\hat{\beta}^M$  is adjusted for the within-center correlations (Zhou et al., 2012).

To identify important variables for the marginal cumulative incidence function, we propose to penalized the log-pseudo-partial likelihood function. The objective function is defined as

$$Q^M(\beta) = l^M(\beta) - K \sum_{j=1}^d p_\lambda(|\beta_j|). \quad (6)$$

The penalized estimator maximizes the objective function (6) and is denoted as

$$\tilde{\beta}^M = \arg \max Q^M(\beta).$$

The marginal PSH model regards center as the sampling unit, we hence formulate the objective function (6) with a scale of  $K$  for the penalty term. With such a formulation, we are able to show selection consistency and the oracle properties of ALASSO, SCAD, and MCP as  $K \rightarrow \infty$ . The theorem and proofs are included in Appendix B.

The efficient CD algorithm can be employed to optimize the objective function (6), because in the penalized marginal PSH model, this algorithm minimizes  $Q^M(\beta) \approx K^{-1}(\mathbf{y} - \boldsymbol{\eta})^T(-\partial^2 l^M / \partial \boldsymbol{\eta} \partial \boldsymbol{\eta}^T)(\mathbf{y} - \boldsymbol{\eta}) + \sum_{j=1}^d p_\lambda(|\beta_j|)$ , where  $\boldsymbol{\eta} = \mathbf{Z}\beta$ ,  $\mathbf{Z}$  is the  $n \times d$  design matrix, and  $\mathbf{y} = \boldsymbol{\eta} - (\partial^2 l^M / \partial \boldsymbol{\eta} \partial \boldsymbol{\eta}^T)^{-1}(\partial l^M / \partial \boldsymbol{\eta})$ . For a data set with a moderate sample size, the  $n \times n$  matrix  $\partial^2 l^M / \partial \boldsymbol{\eta} \partial \boldsymbol{\eta}^T$  is positive definite and thus can be inverted. Since  $Q^M(\beta)$  differs from the objective function of the penalized PSH model only by the scale of the penalty term, we follow the implementation procedure presented in Fu et al. (2015) with adjusted penalty terms. The tuning parameter can be selected by  $\text{BIC}(\lambda) = -2l^M(\tilde{\beta}^M) + \log(K)\text{DF}_\lambda$ , where  $\text{DF}_\lambda = \text{tr}\{\mathbf{Z}^T \hat{\mathbf{D}}^M \mathbf{Z} - K \mathbf{A}_\lambda\}^{-1} \mathbf{Z}^T \hat{\mathbf{D}}^M$  and  $\hat{\mathbf{D}}^M$  is a diagonal matrix with entries of  $h_{ki} = \partial^2 l^M / \partial \eta_{ki} \partial \eta_{ki}^T|_{\beta=\tilde{\beta}^M}$ ,  $i = 1, \dots, n_k$ ,  $k = 1, \dots, K$ .

Center effects (or within-center correlations) are accommodated in the variance-covariance estimator of  $\tilde{\beta}^M$ , which is defined as

$$\text{cov}(\tilde{\beta}^M) = \{\mathbf{Z}^T \hat{\mathbf{D}}^M \mathbf{Z} - K \mathbf{A}_\lambda(\tilde{\beta}^M)\}^{-1} \text{cov}(\mathbf{U}^M(\tilde{\beta}^M)) \{\mathbf{Z}^T \hat{\mathbf{D}}^M \mathbf{Z} - K \mathbf{A}_\lambda(\tilde{\beta}^M)\}^{-1},$$

where  $\mathbf{U}^M(\beta)$  is the score function of  $l^M(\beta)$  accommodating the within-center correlations. Since we assume event times are independent,  $\mathbf{U}^M(\beta)$  is equivalent to the score function of the ordinary PSH model. However, the standard covariance of  $\mathbf{U}^M(\beta)$  proposed by Fine and Gray (1999) may no longer be valid due to the possible dependence among patients within a center (Lee et al., 1992; Zhou et al., 2012). Zhou et al. (2012) showed that  $\mathbf{U}^M(\beta)$  is asymptotically equivalent to a sum of independent identically distributed random variables. Therefore, the covariance of  $\mathbf{U}^M(\beta)$  can be consistently estimated, in a manner robust to the within-cluster correlations. The explicit expression of  $\text{cov}\{\mathbf{U}^M(\beta)\}$  can be found in Zhou et al. (2012).



## 2.4 Extension to Group Variable Selection

Among the potential risk factors for graft failure, some have multiple categories and can be represented by a group of dummy variables. For example, the mismatch score of human leukocyte antigen B (HLA-B) has three levels (0, 1, and 2) and the peak panel reactive antibody is categorized into four levels ( $=0$ , 1-50, 51-80,  $>80$ ). The selection of such factors corresponds to the selection of groups of variables. Our methods can be easily adapted to group variable selection by adjusting the penalty function.

Assume there are  $J$  groups of variables and each group is of size  $d_j, j = 1, \dots, J$ . The vector of regression coefficients can be divided into  $J$  sub-vectors,  $\boldsymbol{\beta}^T = (\boldsymbol{\beta}_1^T, \dots, \boldsymbol{\beta}_J^T)$ . We replace the penalty functions in objective functions (3, 6) with their group version,  $p(\|\boldsymbol{\beta}_j\|; d_j^{1/2}\lambda)$ , where  $\|\boldsymbol{\beta}_j\| = (\boldsymbol{\beta}_j^T \boldsymbol{\beta}_j)^{1/2}$  and  $d_j$  is a scalar for adjusting group sizes,  $j = 1, \dots, J$ . The case  $d_1 = \dots = d_J = 1$  denotes individual variable selection. Following Fu et al. (2015), the penalized estimators with group penalties are expected to behave similarly to their individual versions and optimization procedures can be developed accordingly.

## 3 Simulation

Three sets of simulations are conducted to assess the performance of the penalized stratified PSH model ('penalized stratified model' hereafter) and the penalized marginal PSH model ('penalized marginal model' hereafter). Results on the maximum partial likelihood estimator (MPLE) and the oracle estimators are also reported. Here the oracle estimator is obtained by fitting the underlying model. In the first simulation, the number of centers is fixed at three and the center size is relatively large. The performance of the penalized stratified model for regular stratification is evaluated. The penalized marginal method is not assessed due to the small number of centers. In the second set, the center number is large while the center size is small. The performance of the penalized stratified model for high stratification and the penalized marginal model is evaluated. In the third set, both the number of centers and the center size are moderate. The performance of the penalized stratified model for regular and high stratification as well as the penalized marginal model is assessed.

In the first two sets of simulations, we also applied the penalized PSH model with log-normal frailties ('penalized frailty model' hereafter) (Ha et al., 2014b) and compare its performance with the penalized stratified model. The penalized frailty model is a conditional approach that models the center effect through frailties. For center  $k$ , the subdistribution hazard conditional on frailties  $\mathbf{v}_1 = (v_{11}, \dots, v_{1k}, \dots, v_{1K})$  has the following form

$$\lambda_{1k}(t; \mathbf{Z}_{ki}, v_{1k}) = \lambda_{10}(t) v_{1k} \exp(\boldsymbol{\beta}_1^T \mathbf{Z}_{ki}), \quad (7)$$

where  $\mathbf{v}_1$  has two assumptions: (1)  $\mathbf{v}_1$  follows a log-normal distribution and (2)  $\mathbf{v}_1$  acts proportionally on the baseline subdistribution hazard. Through penalizing the model in equation (7), Ha et al. (2014b) demonstrated that the model performs well through simulations where both assumptions on  $\mathbf{v}_1$  are satisfied. In our simulations,

we show the limitation of the penalized frailty model due to its restrictive assumptions, and also demonstrate the flexibility of the penalized stratified model, which does not require explicit modeling of the center effect.

The performance of variable selection methods is assessed by four measures: the average numbers of correctly (C) and incorrectly (IC) selected zero coefficients, the percentage of identifying the true model (Pcorr), and the median of mean squared error (MMSE). Values of C and IC characterize the performance in shrinking unimportant variables to zero and selecting important variables respectively. The mean squared error (MSE) is defined as  $(\tilde{\beta}^S - \beta_0)\mathbf{I}(\tilde{\beta}^S - \beta_0)$  or  $(\tilde{\beta}^M - \beta_0)\mathbf{I}(\tilde{\beta}^M - \beta_0)$  for assessing the model error, where  $\mathbf{I}$  is the population correlation matrix (Tibshirani, 1997).

### 3.1 A Small Number of Large Centers

In this scenario, the center indicator  $\xi$  is randomly sampled from  $\{1, 2, 3\}$ . For each center, we follow the procedure described in Fine and Gray (1999) to simulate data. Eight covariates  $Z_1, \dots, Z_8$  are included in the model, and they are marginally standard normal with pairwise correlations  $\text{corr}(Z_i, Z_j) = \rho^{|i-j|}$ , where  $\rho = 0.5$ . For cause 1, the vector of regression coefficients is  $\beta_1 = (0.8, 0, 0, 1, 0, 0, 0.6, 0)^T$ , implying that the underlying model includes  $Z_1, Z_4$ , and  $Z_7$ . For cause 2, the regression parameter is  $\beta_2 = -\beta_1$ . The baseline subdistribution hazards for the three centers have different parametric forms and their cumulative incidence functions for cause 1 are defined as follows

$$\begin{aligned} F_{11}(t; \mathbf{Z}_{1i}) &= 1 - \{1 - p \times \Phi(\frac{\log(t) - 1}{0.25})\}^{\exp(\beta_1^T \mathbf{Z}_{1i})}, \\ F_{21}(t; \mathbf{Z}_{2i}) &= 1 - [1 - p\{1 - \exp(-0.018e^t + 0.018)\}]^{\exp(\beta_1^T \mathbf{Z}_{2i})}, \\ F_{31}(t; \mathbf{Z}_{3i}) &= 1 - [1 - p\{1 - \exp(-t^5)\}]^{\exp(\beta_1^T \mathbf{Z}_{3i})}, \end{aligned}$$

which are a log-normal mixture, a Gompertz mixture, and a Weibull mixture with mass  $1 - p$  at  $\infty$  when  $\mathbf{Z}_{ki} = 0$ . The value of  $p$  is 0.6. Their corresponding cumulative incidence functions conditional on cause 2 follow exponential distributions with rates  $5 \exp(\beta_2^T \mathbf{Z}_{1i})$ ,  $10 \exp(\beta_2^T \mathbf{Z}_{2i})$ , and  $2 \exp(\beta_2^T \mathbf{Z}_{3i})$ . Censoring times are independently generated from a Uniform  $(0, 9)$  distribution to achieve a censoring rate of 25%–30%. Note under this setting, the penalized frailty model may not perform well due to the restrictive form of the subdistribution hazard. According to the model in equation (7), baseline subdistribution hazards of the three centers only differ by the scalar  $v_{1k}$ , while the ones in our scenario have distinct shapes.

Table 1 shows the selection results of the penalization methods for the regularly stratified PSH model and the PSH frailty model with sample sizes of 200 and 400. All penalties outperform the MPLE. In particular, the performance of ALASSO, SCAD, and MCP in identifying the underlying model and parameter estimation is close to the oracle estimator. LASSO tends to select over-fitted models with higher false positive rates than the other three penalties. Regardless of penalty choices, the penalized frailty model tends to select unimportant variables while dropping the

Table 1: Selection results of the penalized stratified and frailty model based on 100 replications with  $p = 0.6$ . Center number  $K = 3$ . Sample size  $n = 200$  and 400. The censoring rate is 28% and the event rate is 40%.

Penalty	Model	n=200				n=400			
		C	IC	Pcorr	MMSE	C	IC	Pcorr	MMSE
MPLE	Stratified	0	0	0%	0.133	0	0	0%	0.060
	Frailty	0	0	0%	0.280	0	0	0%	0.219
LASSO	Stratified	3.37	0	23%	0.112	3.76	0	29%	0.055
	Frailty	3.50	0.05	23%	0.228	3.78	0	32%	0.180
ALASSO	Stratified	4.75	0.01	79%	0.064	4.92	0	92%	0.028
	Frailty	4.57	0.08	69%	0.159	4.77	0	83%	0.118
SCAD	Stratified	4.92	0	92%	0.052	4.93	0	93%	0.027
	Frailty	4.74	0.12	81%	0.100	4.85	0	86%	0.100
MCP	Stratified	4.92	0	92%	0.056	4.93	0	93%	0.026
	Frailty	4.76	0.12	84%	0.098	4.85	0	86%	0.100
Oracle	Stratified	5	0	100%	0.044	5	0	100%	0.021
	Frailty	5	0	100%	0.095	5	0	100%	0.092

C: the average number of coefficients that are correctly set to zero; IC: the average number of coefficients that are incorrectly set to zero; Pcorr: the percentage of identifying the true model; MMSE: median of mean squared error.

important ones. Its model error is twice the error of the penalized stratified model when  $n = 200$  and five times the error when  $n = 400$ .

### 3.2 A Large Number of Small Centers

In this scenario, center numbers are 100 and 200. The center size is either 2 or uniformly sampled from  $\{2, 3, 4, 5\}$ . For center  $k$ , we consider a conditional subdistribution hazard in the form of the frailty model,  $\lambda_{1k}(t; \mathbf{Z}_{ki}, v_{1k}) = \lambda_{10}(t)v_{1k} \exp(\beta_1^T \mathbf{Z}_{ki})$ , where  $\lambda_{10}(t) = e^{-t}$  and  $v_{1k}$  is generated from a positive stable distribution with parameter  $\alpha_1$ . A smaller  $\alpha_1$  is associated with a higher within-center correlation, implying that patients within a center are more similar. Under this setting, the assumption that  $v_{1k}$  follows a log-normal distribution in the penalized frailty model is violated. Covariates  $Z_1, \dots, Z_8$  are marginally standard normal with pairwise correlations  $\rho^{|i-j|}$ , where  $\rho = 0.5$ . The cumulative incidence function conditional on frailties and covariates is  $F_{1k}(t; \mathbf{Z}_{ki}, v_{1k}) = 1 - \exp\{e^{-t}v_{1k} \exp(\beta_1^T \mathbf{Z}_{ki})\}$ . Given cause 2, the conditional cumulative incidence function is assumed to be exponential with a rate of  $v_{2k} \exp(\beta_2^T \mathbf{Z}_{ki})$ , where  $\beta_2 = -\beta_1$ . The frailty  $v_{2k}$  is generated from a positive stable distribution with parameter  $\alpha_2$ . Data are then simulated based on the two conditional cumulative incidence functions.

From the conditional cumulative incidence function, we can derive the marginal cumulative incidence function and the marginal subdistribution hazard by integrating out the frailties. The resulting marginal subdistribution hazard also satisfies the

Table 2: Selection results of the penalized stratified and frailty model based on 100 replications for  $\alpha_1 = 0.4$  and  $0.7$ . Center number  $K = 100$  and  $200$ . Center size  $n_k = 2$  and  $n_k \in \{2, 3, 4, 5\}$ . The censoring rate is 27% and the event rate is 46%. Numbers in the parentheses are ratios of MMSE of the penalized estimator to the oracle estimator.

$n_k$	$K$	Stratified										Frailty		
		$\alpha_1 = 0.4$					$\alpha_1 = 0.7$					$\alpha = 0.7$		
		penalty	C	IC	Pcorr	MMSE	C	IC	Pcorr	MMSE(ratio)	C	IC	Pcorr	MMSE(ratio)
2	100	MPLE	0	0	0%	1.184	0	0	0%	1.160 (2.86)	0	0	0%	0.176 (2.63)
		LASSO	3.93	0.41	29%	0.616	3.76	0.38	30%	0.557 (1.37)	3.12	0.02	15%	0.195 (2.92)
		ALASSO	4.45	0.61	46%	0.494	4.42	0.50	47%	0.541 (1.33)	4.27	0.06	49%	0.125 (1.87)
		SCAD	4.36	0.81	46%	0.940	4.53	0.81	43%	0.964 (2.37)	4.60	0.09	69%	0.093 (1.40)
		MCP	4.19	0.68	44%	0.986	4.52	0.80	42%	0.964 (2.37)	4.60	0.08	69%	0.102 (1.52)
		Oracle	5	0	100%	0.283	5	0	100%	0.406 (1.00)	5	0	100%	0.067 (1.00)
	200	MPLE	0	0	0%	0.365	0	0	0%	0.406 (3.09)	0	0	0%	0.098 (2.18)
		LASSO	3.58	0.08	22%	0.307	3.54	0.03	17%	0.320 (2.44)	3.34	0	20%	0.116 (2.58)
		ALASSO	4.60	0.18	57%	0.226	4.58	0.18	59%	0.241 (1.84)	4.69	0	76%	0.075 (1.67)
		SCAD	4.79	0.35	71%	0.218	4.83	0.34	69%	0.287 (2.18)	4.76	0	81%	0.060 (1.34)
		MCP	4.79	0.36	72%	0.218	4.82	0.33	69%	0.280 (2.13)	4.76	0	81%	0.060 (1.34)
		Oracle	5	0	100%	0.102	5	0	100%	0.131 (1.00)	5	0	100%	0.045 (1.00)
	{2,3,4,5}	MPLE	0	0	0%	0.169	0	0	0%	0.164 (2.80)	0	0	0%	0.085 (2.75)
		LASSO	3.66	0	20%	0.161	3.61	0	22%	0.178 (3.04)	3.34	0	19%	0.100 (3.23)
		ALASSO	4.70	0.05	72%	0.104	4.76	0.02	79%	0.097 (1.65)	4.58	0	68%	0.058 (1.89)
		SCAD	4.86	0.06	86%	0.060	4.90	0.06	88%	0.060 (1.02)	4.70	0	75%	0.051 (1.63)
		MCP	4.87	0.06	87%	0.060	4.90	0.05	87%	0.060 (1.02)	4.70	0	75%	0.051 (1.63)
		Oracle	5	0	100%	0.049	5	0	100%	0.058 (1.00)	5	0	100%	0.031 (1.00)
		MPLE	0	0	0%	0.075	0	0	0%	0.078 (2.47)	0	0	0%	0.042 (2.45)
		LASSO	3.49	0	23%	0.087	3.76	0	29%	0.080 (2.55)	3.44	0	18%	0.047 (2.77)
		ALASSO	4.85	0	87%	0.038	4.82	0	84%	0.041 (1.29)	4.72	0	79%	0.024 (1.42)
		SCAD	4.94	0	94%	0.030	4.92	0	93%	0.034 (1.08)	4.76	0	79%	0.022 (1.31)
		MCP	4.94	0	94%	0.030	4.92	0	93%	0.034 (1.08)	4.78	0	80%	0.022 (1.27)
		Oracle	5	0	100%	0.028	5	0	100%	0.032 (1.00)	5	0	100%	0.017 (1.00)

Notation is the same as Table 1.

proportional hazard assumption (Zhou et al., 2012; Logan et al., 2011). By Laplace transformation,

$$F_1(t; \mathbf{Z}_{ki}) = \int_0^t F_1(u; \mathbf{Z}_{ki}, v_{1k}) dF_{V_{1k}}(u) = 1 - \exp\{-M_0^{\alpha_1}(t)e^{(\beta_1^*)^T \mathbf{Z}_{ki}}\}, \quad (8)$$

$$u_1(t; \mathbf{Z}_{ki}) = \alpha_1 M_0^{\alpha_1-1}(t) \lambda_{10}(t) \exp\{(\beta_1^*)^T \mathbf{Z}_{ki}\}, \quad (9)$$

where  $M_0(t) = \int_0^t \lambda_{10}(s) ds$ , and  $\beta_1^* = \alpha_1 \beta_1$ . Correspondingly, the marginal cumulative incidence function given cause 2 is exponential with rate  $\alpha_2 t^{\alpha_2-1} \exp\{(\beta_2^*)^T \mathbf{Z}_{ki}\}$  and  $\beta_2^* = \alpha_2 \beta_2$ .

Table 2 summarizes the selection results of the penalization method for the highly stratified PSH model and the PSH frailty model, where  $\beta_1 = (0.8, 0, 0, 1, 0, 0, 0.6, 0)$  and  $\alpha_1 = \alpha_2 = 0.4$  or  $0.7$ . The penalized frailty model is only applied for  $\alpha_1 = 0.7$ , because when  $\alpha_1 = 0.4$ , the algorithm can not converge under the mis-specification of the frailty distribution. We additionally include relative MMSE, which is defined as the ratio of the MMSE of the penalized estimator to the oracle estimator.

Overall, the performance of the penalized stratified model is improved as the sample size increases, but invariant to the change of within-center correlations. When the center size is 2 such as in the matched cohort study, error rates of identifying

important variables and model errors are much higher than the oracle estimator. Because a center only contributes to the partial likelihood when the failure from the cause of interest is observed for a subject while the other subject has not failed from any causes or has already failed from the competing risks, a great amount of information is discarded, leading to the worsened performance. As the center size increases to  $\{2, 3, 4, 5\}$ , the accuracy in model selection and parameter estimation is considerably improved. SCAD and MCP consistently beat the other penalties and perform similarly to the oracle estimator in all scenarios.

Comparing the penalized stratified and the penalized frailty models for  $\alpha_1 = 0.7$ , the former outperforms the latter in eliminating unimportant variables and producing small relative MMSEs when the center size is in  $\{2, 3, 4, 5\}$ , but underperforms when the center size is two. Note that the penalized frailty model has smaller absolute MMSEs than the penalized stratified model for all penalties, MPLE, and the oracle estimator. It is possible that the parametric modeling of frailties using the log-normal distribution can roughly capture the positive stable distribution, leading to less variation in penalized estimators than the penalized stratified model.

Table 3 shows the simulation results for the penalized marginal PSH model with  $\beta_1^* = (0.8, 0, 0, 1, 0, 0, 0.6, 0)^T$  and  $\alpha_1 = \alpha_2 = 0.4$  or  $0.7$ . For both center sizes, the performance is similar. As the number of centers increases, the accuracy of variable selection and parameter estimation is improved. Three penalties, ALASSO, SCAD, and MCP have close performance to the oracle estimator for  $K = 200$ . When the within-center correlation is larger ( $\alpha_1 = 0.4$ ), selected models have less correctly selected zeros and higher model errors versus when the correlation is smaller ( $\alpha_1 = 0.7$ ), but the difference is minor.

It should be noted that the penalized stratified model and the penalized marginal model were applied to data that were simulated using different regression parameters (*i.e.*,  $\beta_1$ ). In the simulations for the penalized stratified model, data were simulated based on the center-specific subdistribution hazard  $\lambda_{1k}(t; \mathbf{z}_{ki}, v_{1k}) = \lambda_{10}(t)v_{1k} \exp(\beta_1^T \mathbf{z}_{ki})$  with  $\beta_1 = (0.8, 0, 0, 1, 0, 0, 0.6)^T$ . In the simulations for the penalized marginal model, we set  $\beta_1^* = (0.8, 0, 0, 1, 0, 0, 0.6)^T$ , and data were generated using the center-specific subdistribution hazard with  $\beta_1 = \alpha_1^{-1} \beta_1^*$ . Since  $0 < \alpha_1 < 1$ ,  $\beta_1$  is larger than  $\beta_1^*$  in magnitude, implying that the covariate effects for the underlying marginal PSH model is smaller than those for the underlying stratified PSH model. When the penalized stratified model and the penalized marginal model are applied to the same data set, the latter is more likely to select a larger model than the former, because the penalization method tends to select a larger model when the covariate effects are smaller (Tibshirani, 1997; Zhang and Lu, 2007).

### 3.3 A Moderate Number of Moderately Sized Centers

We follow Section 3.2 to simulate competing risks data with 50 centers and a center size of 25 or 50. Table 4 summarizes the selection results of the penalized stratified models with both regular and high stratification, where  $\beta_1 = (0.8, 0, 0, 1, 0, 0, 0.6, 0)$ ,  $\alpha_1 = \alpha_2 = 0.4$  or  $0.7$ . When both the number of center and the center size are moderate, the performance of the penalized regularly stratified model is similar to

Table 3: Selection results of the penalized marginal model based on 100 replications with  $\alpha_1 = 0.4$  and  $0.7$ . Center number  $K = 100$  and  $200$ . Center size  $n_k = 2$  and  $n_k \in \{2, 3, 4, 5\}$ . The censoring rate is 29% and the event rate is 43%.

$n_k$	$K$	penalty	$\alpha_1 = 0.4$				$\alpha_1 = 0.7$			
			C	IC	Pcorr	MMSE	C	IC	Pcorr	MMSE
2	100	MPLE	0	0	0%	0.166	0	0	0%	0.171
		LASSO	3.55	0	26%	0.092	3.39	0	19%	0.130
		ALASSO	4.73	0	77%	0.048	4.74	0	79%	0.064
		SCAD	4.79	0	82%	0.040	4.83	0	86%	0.054
		MCP	4.83	0	85%	0.039	4.80	0	82%	0.054
		Oracle	5	0	100%	0.030	5	0	100%	0.044
	200	MPLE	0	0	0%	0.076	0	0	0%	0.066
		LASSO	3.29	0	19%	0.063	3.50	0	20%	0.069
		ALASSO	4.89	0	89%	0.026	4.88	0	90%	0.023
		SCAD	4.90	0	92%	0.021	4.92	0	93%	0.017
		MCP	4.91	0	92%	0.022	4.89	0	90%	0.018
		Oracle	5	0	100%	0.020	5	0	100%	0.016
(2,3,4,5)	100	MPLE	0	0	0%	0.099	0	0	0%	0.097
		LASSO	3.38	0	20%	0.066	3.56	0	22%	0.060
		ALASSO	4.81	0	87%	0.032	4.84	0	85%	0.035
		SCAD	4.80	0	87%	0.031	4.88	0	91%	0.031
		MCP	4.81	0	87%	0.030	4.84	0	85%	0.032
		Oracle	5	0	100%	0.028	5	0	100%	0.029
	200	MPLE	0	0	0%	0.050	0	0	0%	0.039
		LASSO	3.48	0	18%	0.036	3.73	0	28%	0.032
		ALASSO	4.93	0	93%	0.017	4.95	0	95%	0.016
		SCAD	4.97	0	97%	0.015	4.96	0	96%	0.014
		MCP	4.95	0	95%	0.016	4.96	0	96%	0.014
		Oracle	5	0	100%	0.014	5	0	100%	0.014

Notation is the same as Table 1.

that of the penalized highly stratified model. Similar to the observations in Table 2, the within-center correlation does not affect the performance of the penalized stratified model. Three penalties, ALASSO, SCAD, and MCP, perform similarly to the oracle estimator for both  $n_k = 25$  and  $50$ , due to the large sample size. Notably, the performance of ALASSO for the penalized highly stratified model is improved compared to its performance when the center size is small in Section 3.2. Because a larger center contributes more information, the MPLE, *i.e.* the data-adaptive weights for the ALASSO, is more accurate.

Table 4 also demonstrates the selection results for the penalized marginal model with the same settings of center sizes, center numbers, and within-center correlations. Data were simulated with  $\beta_1^* = (0.8, 0, 0, 1, 0, 0, 0.6, 0)^T$  as in Section 3.2. When the number of centers is moderate ( $K = 50$ ), the penalized marginal model performs worse than the scenario when  $K = 100$  or  $200$  in Section 3.2.

In the above simulations in Section 3.1-3.3, censoring times were generated independently from event times, failure causes, and covariates. When censoring times are covariate-dependent, the simulation results suggest that the proposed penalization

methods perform similarly to the situation when censoring times and covariates are independent. This may be due to the inverse probability of censoring weighting techniques (Robins and Rotnitzky, 1992) used in the stratified PSH model (Zhou et al., 2011), and the marginal inverse probability of censoring weight applied in the marginal PSH model (Zhou et al., 2012), which allows possible dependence between covariates and censoring times (Fine and Gray, 1999). Refer to Appendix D.

Table 4: Selection results of the penalized stratified model based on 100 replications for  $\alpha_1 = 0.4$  and  $0.7$ . Center number  $K = 50$ . Center size  $n_k = 25$  and  $50$ . The censoring rate is 26-27% and the event rate is 45-49%.

Model	K	$n_k$	$\alpha = 0.4$				$\alpha = 0.7$			
			C	IC	Pcorr	MMSE	C	IC	Pcorr	MMSE
Regularly Stratified	50	25	MPLE	0	0	0	0.018	0	0	0.017
			LASSO	3.56	0	0.2	0.020	3.67	0	0.22
			ALASSO	4.96	0	0.96	0.007	4.93	0	0.94
			SCAD	4.97	0	0.97	0.005	4.97	0	0.97
			MCP	4.97	0	0.97	0.005	4.97	0	0.97
			Oracle	5	0	1	0.005	5	0	1
		50	MPLE	0	0	0	0.008	0	0	0.006
			LASSO	3.81	0	0.2	0.009	3.77	0	0.33
			ALASSO	4.95	0	0.95	0.003	4.97	0	0.97
			SCAD	4.98	0	0.98	0.003	4.94	0	0.94
			MCP	4.98	0	0.98	0.003	4.94	0	0.94
			Oracle	5	0	1	0.003	5	0	1
	Highly Stratified	25	MPLE	0	0	0	0.018	0	0	0.017
			LASSO	3.57	0	0.21	0.021	3.67	0	0.23
			ALASSO	4.96	0	0.96	0.007	4.92	0	0.93
			SCAD	4.97	0	0.97	0.005	4.97	0	0.97
			MCP	4.97	0	0.97	0.005	4.97	0	0.97
			Oracle	5	0	1	0.005	5	0	1
		50	MPLE	0	0	0	0.008	0	0	0.006
			LASSO	3.78	0	0.18	0.010	3.76	0	0.35
			ALASSO	4.95	0	0.95	0.003	4.97	0	0.97
			SCAD	4.98	0	0.98	0.003	4.94	0	0.94
			MCP	4.98	0	0.98	0.003	4.94	0	0.94
			Oracle	5	0	1	0.003	5	0	1
Marginal	50	25	MPLE	0	0	0	0.033	0	0	0.026
			LASSO	2.52	0	0	0.025	3.04	0	0.13
			ALASSO	4.76	0	0.81	0.017	4.86	0	0.87
			SCAD	4.70	0	0.83	0.016	4.71	0	0.85
			MCP	4.75	0	0.83	0.018	4.75	0	0.84
		50	Oracle	5	0	1	0.014	5	0	1
			MPLE	0	0	0	0.025	0	0	0.018
			LASSO	2.60	0	0	0.018	3.39	0	0.15
			ALASSO	4.77	0	0.82	0.016	4.85	0	0.88
			SCAD	4.69	0	0.84	0.016	4.77	0	0.88
			MCP	4.76	0	0.84	0.017	4.85	0	0.88
			Oracle	5	0	1	0.013	5	0	1
										0.008

Notation is the same as Table 1.

## 4 Application

In the KDRI study, a subset of UNOS data was used (Rao et al., 2009), including patients who received deceased donor kidney transplants in 1995-2005 with the following exclusion criteria: recipients with previous transplants, with multi-organ transplants, ABO-incompatible, with missing/invalid donor height, with missing/invalid donor weight, or with missing/invalid donor creatinine. Patients were followed from the time of transplantation until the earliest onset of graft failure, DWFG, loss to follow-up, or the conclusion of the observation period (May 1, 2006). A stratified Cox model adjusting for the transplant center effect was fitted and a composite endpoint including graft failure and DWFG was fitted.

We use the UNOS data maintaining the same exclusion criteria, but with longer follow-up time. Patients were followed through March 21, 2013, which incorporates more follow-up information than the KDRI study. We only include patients with complete information on relevant variables. A total of 33,690 patients from 256 centers were obtained, among whom, 10,357 (31%) had graft failures, 7,936 (24%) died with a functioning graft, and 15,397 (46%) were censored. The median number of patients per center is 98.

Thirty-four potential risk factors from the KDRI study are considered in the initial model. Donor factors include donor age, race, sex, height, weight, cause of death, donation after cardiac death, serum creatinine, diabetes status, hypertension status, cigarette users, hepatitis C virus (HCV) positivity. Transplant factors include cold ischemia time, organ sharing (local, regional, national), human leukocyte antigen B (HLA-B) mismatch score (0, 1, 2), HLA-DR mismatch score (0, 1, 2), *en bloc* transplant, double transplant, and ABO compatibility. Recipient factors include recipient age, race, sex, height, weight, primary diagnosis (glomerulonephritis, diabetes, hypertension, failed transplants, congenital anomalies of the kidney and urinary tract (CAKUT), others), diabetes status, pre-transplant blood transfusion, peak panel reactive antibody (PRA) level ( $=0$ , 1-50, 51-80,  $>80$ ), years of renal replacement therapy (RRT) ( $\leq 1$ , 2-3,  $>3$ ), angina pectoris, peripheral vascular disease (PVD), drug-treated chronic obstructive pulmonary disease (COPD), and HCV positivity. Two continuous variables, donor's age and serum creatinine, have nonlinear relationship with the outcome (Rao et al., 2009), we categorize them into three and two levels respectively as in the KDRI study. Hence, grouping structures exist in donor age, peak PRA, serum creatinine, organ sharing, HLA-B and HLA-DR mismatch score, years of RRT, and primary diagnosis. Thirteen extra variables are added. The initial model therefore includes 47 variables.

To account for the center effect and the competing risk, we fit the penalized stratified and the penalized marginal models with four penalties: LASSO, ALASSO, SCAD, and MCP. Grouped variables are selected in or out together. Since the center number and the center size are both large, we consider both the regularly and the highly stratified PSH models. Table 5 presents selected donor and transplant factors and corresponding estimated coefficients. Standard errors are included in the parenthesis. Refer to Appendix C for complete selection results.



Table 5: Variable selection results and estimated regression coefficients using UNOS data. Standard errors are in the parenthesis.

	LASSO	Regularly ALASSO	Stratified SCAD	MCP	LASSO	Highly ALASSO	Stratified SCAD	MCP	LASSO	ALASSO	Marginal SCAD	MCP
<b>Donor Factors</b>												
Age -40 yrs (applies to all ages)	0.012 (0.001)	0.013 (0.001)	0.013 (0.001)	0.012 (0.001)	0.011 (0.001)	0.013 (0.001)	0.013 (0.001)	0.012 (0.001)	0.012 (0.001)	0.013 (0.001)	0.012 (0.001)	0.012(0.001)
Age -18 yrs (applies only if age<18)	-0.010 (0.008)	-0.013 (0.006)	-0.005 (0.007)	-0.005 (0.007)	-0.015 (0.006)	-0.014 (0.005)	-0.005 (0.005)	-0.005 (0.005)	-0.014 (0.008)	-0.018 (0.007)	-0.014 (0.008)	-0.014 (0.008)
Age -50 yrs (applies only if age>50)	0.020 (0.003)	0.018 (0.003)	0.018 (0.003)	0.019 (0.003)	0.018 (0.003)	0.016 (0.002)	0.018 (0.002)	0.019 (0.002)	0.020 (0.003)	0.018 (0.003)	0.020 (0.003)	0.020 (0.003)
African American race	0.170 (0.031)	0.167 (0.031)	0.172 (0.031)	0.168 (0.031)	0.151 (0.023)	0.148 (0.027)	0.174 (0.026)	0.169 (0.027)	0.164 (0.033)	0.157 (0.033)	0.166 (0.033)	0.166 (0.033)
Male	-0.037 (0.026)	-	-	-	-0.042 (0.018)	-	-	-	-0.035 (0.026)	-0.027 (0.023)	-0.034 (0.026)	-0.034 (0.026)
Height: per 10 cm increase	-0.021 (0.013)	-	-0.031 (0.011)	-0.029 (0.011)	-0.008 (0.01)	-	-0.031 (0.008)	-0.028 (0.009)	-0.018 (0.014)	-	-0.019 (0.014)	-0.019 (0.014)
Weight (per 5 kg increase if <80 kg)	-0.227 (0.06)	-0.311 (0.052)	-0.248 (0.059)	-0.241 (0.059)	-0.169 (0.048)	-0.215 (0.043)	-0.251 (0.05)	-0.244 (0.045)	-0.213 (0.064)	-0.235 (0.059)	-0.220 (0.064)	-0.22 (0.064)
Donation after cardiac death	-	-	-	-	-	-	-	-	-	-	-	-
Cause of death: stroke	0.061 (0.025)	0.073 (0.024)	-	0.067 (0.024)	0.067 (0.021)	0.040 (0.019)	-	0.069 (0.022)	0.066 (0.025)	0.053 (0.025)	0.066 (0.025)	0.066 (0.025)
Serum creatinine-1 (applies to all Cr values )	0.195 (0.036)	0.174 (0.035)	0.183 (0.035)	0.186 (0.035)	0.150 (0.026)	0.107 (0.028)	0.183 (0.022)	0.187 (0.029)	0.192 (0.035)	0.155 (0.035)	0.196 (0.035)	0.196 (0.035)
Serum creatinine-1 (applies if Cr>1.5 )	-0.189 (0.05)	-0.165 (0.049)	-0.176 (0.049)	-0.179 (0.049)	-0.143 (0.034)	-0.099 (0.036)	-0.177 (0.032)	-0.180 (0.036)	-0.185 (0.046)	-0.148 (0.046)	-0.189 (0.046)	-0.189 (0.046)
Diabetic	0.233 (0.047)	0.237 (0.047)	0.228 (0.047)	0.232 (0.047)	0.212 (0.039)	0.191 (0.038)	0.231 (0.034)	0.235 (0.036)	0.242 (0.05)	0.229 (0.049)	0.245 (0.05)	0.245 (0.05)
Hypertensive	0.137 (0.026)	0.139 (0.026)	0.151 (0.026)	0.138 (0.026)	0.132 (0.02)	0.130 (0.021)	0.150 (0.018)	0.136 (0.022)	0.142 (0.027)	0.143 (0.027)	0.142 (0.027)	0.142 (0.027)
Cigarette users	0.027 (0.021)	-	-	-	0.017 (0.013)	-	-	-	0.024 (0.018)	-	0.025 (0.018)	0.025 (0.018)
Positive HCV status	0.098 (0.068)	-	-	-	0.070 (0.048)	-	-	-	0.133 (0.064)	0.055 (0.064)	0.135 (0.064)	0.135 (0.064)
<b>Transplant Factors</b>												
Cold ischemic time (ref=20 hr)	0.003 (0.001)	-	-	-	0.002 (0.001)	-	-	-	0.004 (0.002)	0.002 (0.001)	0.004 (0.002)	0.004 (0.002)
Organ sharing (ref=local)												
Regional	0.061 (0.037)	-	-	-	0.045 (0.022)	-	-	-	0.030 (0.038)	-	0.031 (0.038)	0.031 (0.038)
National	-0.052 (0.031)	-	-	-	-0.038 (0.027)	-	-	-	-0.049 (0.037)	-	-0.051 (0.037)	-0.051 (0.037)
HLA-B mismatch												
0 (ref=2 B MM)	-0.155 (0.034)	-0.176 (0.031)	-0.174 (0.031)	-0.174 (0.031)	-0.141 (0.028)	-0.134 (0.025)	-0.174 (0.027)	-0.174 (0.03)	-0.154 (0.039)	-0.158 (0.039)	-0.156 (0.039)	-0.156 (0.039)
1	-0.068 (0.023)	-0.070 (0.023)	-0.069 (0.023)	-0.069 (0.023)	-0.057 (0.019)	-0.051 (0.021)	-0.067 (0.018)	-0.067 (0.017)	-0.055 (0.025)	-0.052 (0.024)	-0.056 (0.025)	-0.056 (0.025)
HLA-DR mismatch												
0 (ref=1 DR MM)	-0.097 (0.027)	-0.103 (0.027)	-0.102 (0.027)	-0.102 (0.027)	-0.087 (0.024)	-0.078 (0.02)	-0.102 (0.024)	-0.102 (0.023)	-0.091 (0.03)	-0.084 (0.029)	-0.092 (0.03)	-0.092 (0.03)
2	0.055 (0.023)	0.057 (0.023)	0.058(0.023)	0.057 (0.023)	0.051 (0.018)	0.047 (0.019)	0.058 (0.017)	0.057 (0.02)	0.063 (0.025)	0.058 (0.025)	0.063 (0.025)	0.063 (0.025)
Transplant year	-0.155 (0.021)	-0.161 (0.021)	-0.165 (0.021)	-0.163 (0.021)	-0.139 (0.018)	-0.139 (0.021)	-0.166 (0.02)	-0.164 (0.02)	-0.151 (0.025)	-0.156 (0.025)	-0.152 (0.025)	-0.151 (0.025)
<i>en bloc</i> transplant	-0.313 (0.117)	-0.285 (0.116)	-0.317 (0.117)	-0.312 (0.117)	-0.209 (0.094)	-0.083 (0.085)	-0.310 (0.094)	-0.304 (0.081)	-0.295 (0.124)	-0.132 (0.122)	-0.304 (0.124)	-0.304 (0.124)
Double kidney transplant	-0.334 (0.093)	-0.329 (0.092)	-0.332 (0.092)	-0.330 (0.092)	-0.247 (0.063)	-0.181 (0.047)	-0.331 (0.067)	-0.330 (0.061)	-0.329 (0.078)	-0.250 (0.078)	-0.338 (0.078)	-0.338 (0.078)
ABO identical	-	-	-	-	-	-	-	-	-0.023 (0.052)	-	-0.026 (0.052)	-0.027 (0.052)

Cr: serum creatinine. HLA: human leukocyte antigen.

For the penalized stratified model, the regularly and the highly stratified select the same variables, with slight differences in estimated effects of covariates. The three oracle penalties, ALASSO, SCAD, and MCP, select similar models, in which 16 out of 18-19 factors are selected by all of them. LASSO selects 27 factors, producing larger models than the others. The penalized marginal model selects larger models than the penalized stratified model, suggesting that the factors that are significant for the marginal cumulative incidence function may not necessarily have effects on the center-specific cumulative incidence function. Across penalties, LASSO, SCAD, and MCP have similar selection results and ALASSO selects a smaller model than the others.

One can choose between the penalized marginal model and the penalized stratified model based on study interests. If the study interest is on the study population, then the penalized marginal model is appropriate, because patients are considered as a representative random sample from the kidney transplant population, and the effects of selected factors have a population-average interpretation (Lee and Nelder, 2004). Alternatively, the penalized stratified model can be applied to account for the varying patient populations across centers. In our analysis, the stratified approach was adopted as in the KDRI study.

The prognostic ability of the selected stratified PSH models in Table 5 can be assessed by a class of discrimination and calibration methods (Wolbers et al., 2009; Schoop et al., 2011). The concordance index (C-index) is a measure of discrimination ranging from 0 to 1 with 1 being perfect discrimination. It is defined as the proportion of all evaluable ordered patients pairs for which prediction and outcomes are concordant. Wolbers et al. (2009) adapted this measure to the competing risks setting and defined an ordered pair as evaluable if the first patient has graft failure at a time point when the second has not experienced any event or has died with a functioning graft. An evaluable ordered pair is concordant if the first patient has higher risk prediction than the second. An alternative measure of discrimination is the D-index, originally proposed by Royston and Sauerbrei (2004) in standard survival analysis. The D-index measures the separation of cumulative incidence curves and can be interpreted as the log-hazard ratio comparing two equal-sized prognostic groups based on dichotomizing the linear predictor from the fitted model. This index is non-negative and a larger value suggests greater discrimination ability. Prediction error (PE) of selected models can be computed as an integrated difference between the observed and the predicted cumulative incidence functions up to a time point (Schoop et al., 2011). Using the results from Fibrinogen Studies (2009), we extend the three measures to the stratified PSH model. The measure of PE is infeasible for the highly stratified PSH model, because the estimator for the baseline cumulative subdistribution hazard can not be obtained due to small strata sizes (Zhou et al., 2011).

We randomly sample 4/5 of the data set as a training set and the rest is a testing set. For regular stratification, the sampling is conducted within centers. For high stratification, one center is regarded as one unit and the sampling is performed upon centers. We obtain parameter estimates using the training set only and then compute the C-index, the D-index, and the 5-year prediction error for the testing set. The

Table 6: Prognostic statistics for penalized stratified models. Standard errors are in the parenthesis.

Stratification	Penalty	No. donor factors	No. transplant factors	C-index	D-index	5-year prediction error
Regular	LASSO	11	7	0.635 (0.007)	0.846 (0.033)	0.145 (0.004)
	ALASSO	7	5	0.636 (0.006)	0.841 (0.036)	0.146 (0.003)
	SCAD	7	5	0.635 (0.006)	0.832 (0.033)	0.146 (0.003)
	MCP	8	5	0.636 (0.006)	0.842 (0.038)	0.146 (0.004)
High	LASSO	11	7	0.636 (0.008)	0.846 (0.037)	-
	ALASSO	7	6	0.636 (0.008)	0.843 (0.038)	-
	SCAD	7	5	0.636 (0.008)	0.841 (0.037)	-
	MCP	8	5	0.636 (0.008)	0.841 (0.037)	-

splitting, estimation and prediction are repeated for 100 times. The averages of the three measures are reported.

Table 6 shows the prognostic statistics for each model. Standard errors are included in the parentheses. All models have similar discrimination power and prediction accuracy. ALASSO and MCP have the highest C-index. LASSO has the highest D-index and the lowest 5-year prediction error. We adopt the regularly stratified PSH model penalized by MCP, because it has satisfactory prognostic ability and model parsimony. Although ALASSO and MCP have similar prognostic statistics and the former has one donor factor (height) less than the latter, it is more reasonable to include both height and weight in the model, since the two are highly correlated and patients' heights can be easily obtained.

Our prognostic model, which we refer to as the kidney donor graft failure index (KDGF), can be constructed in the same way as the KDRI, by using the exponential of the prognostic index (PI). Here PI is a weighted sum of selected donor factors, where the weights are the estimated regression coefficients. Transplant factors are usually not included when assessing generic donor quality (Rao et al., 2009). Since baseline subdistribution hazards are not included, KDGF is a relative cumulative incidence or absolute risk for graft failure compared with a reference donor whose KDGF is 1.00. The reference donor has the following characteristics: 40-year-old, non-African American race, height 170cm, weight more than or equal to 80 kg, cause of death other than cerebrovascular accident, serum creatinine 1.0 mg/dL, non-diabetic, and non-hypertensive. For a particular deceased donor kidney, its PI is calculated by summing PI components for all applicable donor characteristics, which are listed in Table 7. The KDGF is then the exponential of the PI.

All donor factors in KDGF are also included in the KDRI. These factors have the same signs but different magnitudes in the two indices. Two KDRI factors, donation after cardiac death (DCD) and HCV status, are not included the KDGF. Although use of DCD kidneys is associated with increased risk of delayed graft function, there is no significant difference in long-term outcomes between DCD and non-DCD kidneys (Weber et al., 2002; Snøeijs et al., 2010). This might be the reason that DCD is not selected. HCV status is not included in the KDGF, because use of HCV antibody

Table 7: KDGF I donor characteristics and model coefficients

Donor Characteristics	Applies to	KDGF I Prognostic Index (PI)
Age (integer years)	All donors	$0.012 \times (\text{age} - 40)$
	Donor with age $< 18$	$-0.005 \times (\text{age} - 18)$
	Donor with age $> 50$	$0.019 \times (\text{age} - 50)$
Height (cm)	All donors	$-0.029 \times (\text{height} - 170) / 10$
Weight (kg)	All donors with weight $< 80$ kg	$-0.241 \times (\text{weight} - 80) / 5$
Ethnicity	African American donors	0.168
History of Hypertension	Hypertensive donors	0.138
History of Diabetes	Diabetic donors	0.232
Cause of Death (COD)	Donors with COD=cerebrovascular accident	0.067
Serum Creatinine	All donors	$0.186 \times (\text{creat} - 1)$
	Donors with creat $> 1.5$ mg/dL	$-0.179 \times (\text{creat} - 1.5)$

positive donor (HCVD+) kidneys does not significantly increase the risk of graft failure in HCV antibody positive recipients (HCVR+) (Morales et al., 2010), and the majority of HCVD+ kidneys (77% in the UNOS data) are transplanted to HCVR+.

## 5 Discussion

In the analysis of kidney transplant data, variable selection procedures are complicated by the presence of within-center correlations and competing risks. To take the two issues into account, this paper proposes to penalize the stratified and the marginal PSH models, where primary interests are simultaneous variable selection and parameter estimation. Within-center correlations are not explicitly modeled. The penalized marginal model treats the whole center as one unit and achieves good performance when the number of centers is large. The penalized stratified model performs well when either the center size or the center number is large. However, as seen in Table 2 this approach may not be suitable in the analysis of matched data, for which the center size is 2. By applying the proposed methods to the UNOS data from deceased donor kidney transplants, we develop the KDGF I comprised of eight donor characteristics for assessing the relative risk of graft failure. Our analysis results offer a new perspective in quantifying the quality of a kidney organ by considering the competing risk of DWFG, and provide a useful tool in practical kidney transplant research.

The penalized PSH frailty model can be applied to account for the center effect when within-center correlations are of genuine interest, but it may not be appealing in our case where the primary interest is covariate effects. As previously mentioned it is restrictive regarding the type of dependency encompassed and requires the center effect to act proportionally on the subdistribution hazard. Additionally, calculation is cumbersome when the center number is large, due to the involvement of double iterative procedures (Prentice and Cai, 1992). The first iteration calculates frailties and the number of parameters to be estimated is the number of centers. The second iteration conducts the penalization procedure conditional on the frailties. In contrast, the stratified approach only involves the penalization procedure. In the case of the KDGF I study, the number of transplant centers is 256. Using the frailty model

requires extra estimation of 256 parameters, which considerably increases computing time.

The current study was conducted under the setting where  $d < K$  or/and  $d < n_k$  for the stratified approach and  $d < K$  for the marginal approach, while in many applications, data may be high-dimensional, for example,  $d > n$ ,  $n > d > n_k > K$ , or  $n > d > K > n_k$ . Due to the curse of dimensionality, computation may be prohibitive (Fan and Lv, 2010). The proposed penalization methods may not accurately select the underlying model, and their theoretical properties may not be valid. Future work could involve extending the proposed methods to the high-dimensional setting, along with developing efficient and robust computing procedures.

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## Appendix A Large Sample Properties of the Penalized Stratified PSH Model

For simplicity, we shall work on the finite time interval  $[0, \tau]$ . Because of the distinct asymptotic behaviors of the center number and the center size, we write  $\tilde{\beta}^S$  as  $\tilde{\beta}_r^S$  and  $\tilde{\beta}_h^S$  for regularly and highly stratified data respectively. The following conditions are needed to establish the oracle properties.

A1.  $\int_0^\tau \lambda_{k0}(t)dt < \infty$  for  $k = 1, \dots, K$ .

A2. For regularly stratified data,  $\{N_{ki}(\cdot), Y_{ki}(\cdot), \mathbf{z}_{ki}(\cdot)\}_{i=1, \dots, n_k}$  are independently and identically distributed; For highly stratified data,  $\{N_{ki}(\cdot), Y_{ki}(\cdot), \mathbf{z}_{ki}(\cdot), i = 1, \dots, n_k\}_{k=1, \dots, K}$  are independently distributed.

A3. Define

$$s_k^{(p)}(\beta, t) = \lim_{n_k \rightarrow \infty} n_k^{-1} \sum_{i=1}^{n_k} I(C_{ki} \geq t) Y_{ki}(t) \mathbf{z}_{ki}^{\otimes p} \exp(\beta^T \mathbf{z}_{ki}) \quad (10)$$

$$S_k^{(p)}(\beta, t) = n_k^{-1} \sum_{i=1}^{n_k} I(C_{ki} \geq t) Y_{ki}(t) \mathbf{z}_{ki}^{\otimes p} \exp(\beta^T \mathbf{z}_{ki}) \quad (11)$$

$$\hat{S}_k^{(p)}(\beta, t) = n_k^{-1} \sum_{i=1}^{n_k} \hat{w}_{ki}(t) Y_{ki}(t) \mathbf{z}_{ki}^{\otimes p} \exp(\beta^T \mathbf{z}_{ki}) \quad (12)$$

For regularly stratified data, there exists a neighborhood  $\mathcal{B}$  of  $\beta_0$  such that the following conditions are satisfied: (i) there exists a scalar, a vector, and a matrix function  $s_k^{(0)}, \mathbf{s}_k^{(1)}$ , and  $\mathbf{s}_k^{(2)}$  defined on  $\mathcal{B} \times [0, \tau]$  such that  $\sup_{t \in [0, \tau], \beta \in \mathcal{B}} \|\mathbf{s}_k^{(p)}(\beta, t) - \mathbf{s}_k^{(p)}(\beta, t)\| \rightarrow 0$  in probability,  $p = 0, 1, 2$ ; (ii). the matrix  $\Omega_k = \int_0^\tau \mathbf{v}_k(\beta_0, t) s_k^{(0)}(\beta_0, t) \lambda_{0k}(t) dt$  is positive definite, where  $\mathbf{v}_k = \mathbf{s}_k^{(2)} / s_k^{(0)} - (\mathbf{s}_k^{(1)} / s_k^{(0)}) (\mathbf{s}_k^{(1)} / s_k^{(0)})^T$ .

For highly stratified data, the matrix  $\mathbf{I}(\beta_0) = \lim_{K \rightarrow \infty} K^{-1} \sum_{k=1}^K E[\sum_{i=1}^{n_k} \int_0^\tau \{\mathbf{z}_{ki} - \bar{\mathbf{z}}_k(\beta_0, u)\}^{\otimes 2} S^{(0)}(\beta_0, u) \lambda_{0k}(u) du]$  is positive definite.

A4. The penalty function satisfies that  $a_n = O_p(n^{-1/2})$  and  $b_n \rightarrow 0$ .

A5. For regular stratified data,  $p_{\lambda_n}(|\beta|)$  satisfies  $\lim_{n_k \rightarrow \infty} \sqrt{n_k} \inf_{|\beta| \leq Cn^{-1/2}} p'_{\lambda_n}(|\beta|) \rightarrow \infty, k = 1, \dots, K$ .

For highly stratified data,  $p_{\lambda_n}(|\beta|)$  satisfies  $\lim_{K \rightarrow \infty} \bar{m} K^{1/2} \inf_{|\beta| \leq Cn^{-1/2}} p'_{\lambda_n}(|\beta|) \rightarrow \infty$ , where  $\bar{m} = \lim_{K \rightarrow \infty} n/K$ .

### A.1 The Regular Stratified PSH Model

Theorem 1 states selection consistency and the oracle properties for the penalization methods for the regularly stratified PSH model.

**Theorem 1.** For regularly stratified data with finite  $K$ , when  $n \rightarrow \infty$ ,  $n_k \rightarrow \infty$ . The following holds under Condition A.1 - A.5,

- (a.)  $\tilde{\beta}_r^S$  is a root- $n$  consistent estimator for  $\beta_0$ , i.e.  $\|\tilde{\beta}_r^S - \beta_0\| = O_p(n^{-1/2})$ .
- (b.) (Oracle properties) With probability tending to 1, the root- $n$  consistent estimator  $\tilde{\beta}_r^S$  satisfies

(i.) (Sparsity)  $\tilde{\beta}_{2r}^S = \mathbf{0}$

(ii.) (Asymptotic normality)  $n^{1/2} \sum_{k=1}^K \pi_k (\mathbf{\Omega}_{11k} + \mathbf{P}) \{\tilde{\beta}_{1r}^S - \beta_{01} + (\mathbf{\Omega}_{11k} + \mathbf{P})^{-1} \mathbf{b}\} \rightarrow N(\mathbf{0}, \sum_{k=1}^K \pi_k \mathbf{\Sigma}_{11k})$ , where  $p_k = n_k/n \rightarrow \pi_k$ ,  $\mathbf{\Omega}_{11k}$  and  $\mathbf{\Sigma}_{11k}$  are the first  $s \times s$  submatrix of  $\mathbf{\Omega}_k(\beta_0)$  and  $\mathbf{\Sigma}_k(\beta_0)$ , defined in the Appendix.

### A.1.1 Proof of Theorem 1.a

To prove  $\tilde{\beta}_r^S - \beta_0 = O_p(n^{-1/2})$ , it is sufficient to prove that for any positive  $\epsilon$ , there exists a large constant  $C$  such that

$$Pr\left\{ \sup_{\|\mathbf{u}\|=C} Q^S(\beta_0 + \alpha_n \mathbf{u}) < Q^S(\beta_0) \right\} \geq 1 - \epsilon \quad (13)$$

where  $\alpha_n = n^{-1/2} + a_n$ . This means with probability at least  $1 - \epsilon$ , there exists a local maximum such that  $\|\tilde{\beta}_r^S - \beta_0\| = O_p(\alpha_n)$ .

Denoting  $D_n(\mathbf{u}) = \frac{1}{n} \{Q^S(\beta_0 + \alpha_n \mathbf{u}) - Q^S(\beta_0)\}$ , we have

$$D_n(\mathbf{u}) \leq \frac{1}{n} \sum_{k=1}^K \left[ \{l_k(\beta_0 + \alpha_n \mathbf{u}) - l_k(\beta_0)\} - n_k \sum_{j=1}^s \{p_{\lambda_n}(|\beta_{j0} + \alpha_n u_j|) - p_{\lambda_n}(|\beta_{j0}|)\} \right] \quad (14)$$

$$= \frac{1}{n} \sum_{k=1}^K n_k D_{n_k}(\mathbf{u}) \quad (15)$$

where  $D_{n_k}(\mathbf{u}) = \frac{1}{n_k} \{l_k(\beta_0 + \alpha_n \mathbf{u}) - l_k(\beta_0)\} - \sum_{j=1}^s \{p_{\lambda_n}(|\beta_{j0} + \alpha_n u_j|) - p_{\lambda_n}(|\beta_{j0}|)\} := D_1 + D_2$

By Taylor expansion,  $D_1$  is

$$\frac{1}{n_k} \{l_k(\beta_0 + \alpha_n \mathbf{u}) - l_k(\beta_0)\} = \frac{1}{n_k} \left( \frac{\partial l_k(\beta_0)}{\partial \beta} \right)^T \alpha_n \mathbf{u} - \frac{1}{2} \mathbf{u}^T \left\{ -\frac{1}{n_k} \frac{\partial^2 l_k(\beta_0)}{\partial \beta^T \partial \beta} + o_p(1) \right\} \mathbf{u} \alpha_n^2 \quad (16)$$

$$= O_p(n_k^{-1/2}) \alpha_n \mathbf{u} - \frac{1}{2} \alpha_n^2 \mathbf{u}^T \{\mathbf{\Omega}_k(\beta_0) + o_p(1)\} \mathbf{u} \quad (17)$$

$$= O_p(C n_k^{-1/2} \alpha_n) + O_p(C^2 \alpha_n^2) \quad (18)$$

From Fan and Li (2002),  $D_2$  is bounded by  $\sqrt{s}a_n\alpha_n||\mathbf{u}|| + b_n\alpha_n^2||\mathbf{u}^2||$ , which has the order of  $C\alpha_n^2$  if  $b_n \rightarrow 0$ . Define  $r_k = n_k/n \rightarrow \pi_k$ , which is a finite number between 0 and 1. Summing over  $K$  strata,

$$D_n(\mathbf{u}) \leq \sum_{k=1}^K \frac{n_k}{n} \{O_p(Cn_k^{-1/2}\alpha_n) + O_p(C^2\alpha_n^2) + O_p(C\alpha_n^2)\} \quad (19)$$

$$= \sum_{k=1}^K r_k \{O_p(C\alpha_n^2 r_k^{-1/2}) + O_p(C^2\alpha_n^2) + O_p(C\alpha_n^2)\} \quad (20)$$

By choosing a sufficiently large  $C$ ,  $O_p(C^2\alpha_n^2)$  dominates the others. Thus inequality(13) holds.

### A.1.2 Proof of Theorem 1.b. (i)

It is sufficient to show that for any given  $\beta_1$  that is root-n consistent and for any constant  $C$ ,

$$Q^S(\beta_1, \mathbf{0}) = \max_{||\beta_2|| \leq Cn^{-1/2}} Q^S(\beta_1, \beta_2) \quad (21)$$

This is equivalent to show that  $\frac{\partial Q^S(\beta)}{\partial \beta_j} < 0$  for  $0 < \beta_j < Cn^{-1/2}$ , and  $\frac{\partial Q^S(\beta)}{\partial \beta_j} > 0$  for  $-Cn^{-1/2} < \beta_j < 0$  with probability tending to 1 as  $n \rightarrow \infty$ ,  $j = s+1, \dots, d$ .

For stratum  $k$ , define the following

$$X_k(\beta, \tau) = \frac{1}{n_k} \{l_k(\beta) - l_k(\beta_0)\} \quad (22)$$

$$= \frac{1}{n_k} \sum_{i=1}^{n_k} \int_0^\tau \{(\beta - \beta_0)^T \mathbf{Z}_{ki} - \log \frac{\hat{S}_k^{(0)}(\beta, u)}{\hat{S}_k^{(0)}(\beta_0, u)}\} \hat{w}_{ki}(u) dN_{ki}(u) \quad (23)$$

$$A_k(\beta, \tau) = \frac{1}{n_k} \sum_{i=1}^{n_k} \int_0^\tau \{(\beta - \beta_0)^T \mathbf{Z}_{ki} - \log \frac{\hat{S}_k^{(0)}(\beta, u)}{\hat{S}_k^{(0)}(\beta_0, u)}\} \hat{w}_{ki}(u) \lambda_{1k}(u) du \quad (24)$$

$$= \int_0^\tau \{(\beta - \beta_0)^T \hat{\mathbf{S}}_k^{(1)}(\beta_0, u) - \hat{S}_k^{(0)}(\beta_0, u) \log \frac{\hat{S}_k^{(0)}(\beta, u)}{\hat{S}_k^{(0)}(\beta_0, u)}\} \lambda_{1k0}(u) du \quad (25)$$

From Fine and Gray (1999),  $X_k(\beta, \cdot) - A_k(\beta, \cdot)$  is a sum of martingale integrals with respect to locally bounded process. Since  $\lim_{n_k \rightarrow \infty} \hat{\mathbf{S}}^{(p)}(\beta, t) = G(t) \mathbf{s}_k^{(p)}(\beta, t)$ , by condition 3 it follows that for each  $\beta \in \mathcal{B}$ ,

$$A_k(\beta, \tau) \rightarrow f_k(\beta, \tau) = \int_0^\tau \{(\beta - \beta_0)^T \mathbf{s}_k^{(1)}(\beta_0, u) - s_k^{(0)}(\beta_0, u) \log \frac{s_k^{(0)}(\beta, u)}{s_k^{(0)}(\beta_0, u)}\} \lambda_{1k0}(u) du \quad (26)$$

where  $f_k$  has the following properties

$$f_k(\beta_0) = 0, \quad \frac{\partial f_k(\beta_0)}{\partial \beta} = 0, \quad -\frac{\partial^2 f_k(\beta_0)}{\partial \beta \partial \beta^T} = \Omega_k(\beta_0) \quad (27)$$

Then the following holds

$$\frac{1}{n_k}\{l_k(\boldsymbol{\beta}) - l_k(\boldsymbol{\beta}_0)\} = f_k(\boldsymbol{\beta}, \tau) + O_p\left(\frac{\|\boldsymbol{\beta} - \boldsymbol{\beta}_0\|}{\sqrt{n_k}}\right) \quad (28)$$

We also have  $f_k(\boldsymbol{\beta}) = -\frac{1}{2}(\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T\{\Omega_k(\boldsymbol{\beta}_0) + o(1)\}(\boldsymbol{\beta} - \boldsymbol{\beta}_0)$ . By Taylor expansion, we obtain

$$\frac{\partial Q^S(\boldsymbol{\beta})}{\partial \beta_j} = \sum_{k=1}^K \frac{\partial l_k(\boldsymbol{\beta})}{\partial \beta_j} - n_k p'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j) \quad (29)$$

$$= \sum_{k=1}^K n_k \sum_{l=1}^d \frac{\partial^2 f_k(\boldsymbol{\beta}_0)}{\partial \beta_j \partial \beta_l} (\beta_l - \beta_{l0}) + O_p(n_k \|\boldsymbol{\beta} - \boldsymbol{\beta}_0\|^2) - n_k p'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j) \quad (30)$$

$$= \sum_{k=1}^K O_p(n_k n^{-1/2}) + O_p(r_k) - n_k p'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j) \quad (31)$$

$$= \sum_k n_k^{1/2} \{O_p(r_k) - n_k^{1/2} p'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j)\} \quad (32)$$

Since  $\lim_{n_k \rightarrow \infty} \sqrt{n_k} \inf_{\|\boldsymbol{\beta}\| \leq C n^{-1/2}} p'_{\lambda_n}(|\beta|) \rightarrow \infty, k = 1, \dots, K$  in condition C.2, the sign of  $\frac{\partial Q^S(\boldsymbol{\beta})}{\partial \beta_j}$  is completely determined by the sign of  $\beta_j$ .

### A.1.3 Proof of Theorem 1.b. (ii)

It is easy to show that there exists a root-n consistent local maximizer  $\tilde{\boldsymbol{\beta}}_{r1}^S$  of  $Q(\boldsymbol{\beta}_1, \mathbf{0})$ , satisfying equation  $\frac{\partial Q(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}_1} \Big|_{\boldsymbol{\beta}=(\tilde{\boldsymbol{\beta}}_{r1}^S)^T, \mathbf{0}} = 0$ . Denote  $U^S(\boldsymbol{\beta})$  and  $H^S(\boldsymbol{\beta})$  as the score function and the Hessian matrix of  $l^S(\boldsymbol{\beta})$  and they are

$$U^S(\boldsymbol{\beta}) = \sum_{k=1}^K U_k(\boldsymbol{\beta}) = \sum_{k=1}^K \sum_{i=1}^{n_k} \int_0^\infty \left\{ \mathbf{Z}_{ik} - \frac{\hat{\mathbf{S}}_i^{(1)}(\boldsymbol{\beta}, u)}{\hat{\mathbf{S}}_i^{(0)}(\boldsymbol{\beta}, u)} \right\} \hat{w}_{ik}(u) dN_{ik}(u) \quad (33)$$

$$H^S(\boldsymbol{\beta}) = \sum_{k=1}^K H_k(\boldsymbol{\beta}) = \sum_{k=1}^K \sum_{i=1}^{n_k} \int_0^\infty \left[ \frac{\hat{\mathbf{S}}_i^{(2)}(\boldsymbol{\beta}, u)}{\hat{\mathbf{S}}_i^{(0)}(\boldsymbol{\beta}, u)} - \left\{ \frac{\hat{\mathbf{S}}_i^{(1)}(\boldsymbol{\beta}, u)}{\hat{\mathbf{S}}_i^{(0)}(\boldsymbol{\beta}, u)} \right\}^{\otimes 2} \right] \hat{w}_{ik}(u) dN_{ik}(u) \quad (34)$$

For  $j = 1, \dots, s$

$$\begin{aligned} 0 &= \sum_{k=1}^K \frac{\partial l_k(\boldsymbol{\beta})}{\partial \beta_j} \Big|_{\boldsymbol{\beta}=(\tilde{\boldsymbol{\beta}}_1^S)^T, \mathbf{0}} - n_k p'_{\lambda_n}(|\tilde{\beta}_{rj}^S|) \text{sgn}(\tilde{\beta}_{rj}^S) \\ &= \sum_{k=1}^K \frac{\partial l_k(\boldsymbol{\beta}_0)}{\partial \beta_j} - \sum_{l=1}^s \left\{ -\frac{\partial^2 f_k(\boldsymbol{\beta}_0)}{\partial \beta_j \partial \beta_l} + o_p(1) \right\} (\tilde{\beta}_{rl}^S - \beta_{l0}) - \\ &\quad n_k \left( p'_{\lambda_n}(|\beta_{j0}|) \text{sgn}(\beta_{j0}) + \{p''_{\lambda_n}(|\beta_{j0}|) + o_p(1)\} (\tilde{\beta}_{rj}^S - \beta_{j0}) \right) \end{aligned} \quad (35)$$

Denote  $U_{11k}(\boldsymbol{\beta})$  as the first  $s$  elements of the score function  $U_k(\boldsymbol{\beta})$  for stratum  $k$ . As  $n_k \rightarrow \infty$ ,  $n_k^{-1/2} U_{11k}(\boldsymbol{\beta}_0) \rightarrow N(\mathbf{0}, \boldsymbol{\Sigma}_{11k}(\boldsymbol{\beta}_0))$  in distribution, where  $\boldsymbol{\Sigma}_{11k}$  is the first  $s \times s$  submatrix of  $\boldsymbol{\Sigma}_k$ . The explicit formula of  $\boldsymbol{\Sigma}_k$  can be found in Fine and Gray(1999). Thus  $n^{-1/2} \sum_{k=1}^K U_{11k}(\boldsymbol{\beta}_0) = n^{-1/2} \sum_{k=1}^K r_k^{1/2} n_k^{-1/2} U_{11k}(\boldsymbol{\beta}_0) \rightarrow N(\mathbf{0}, \boldsymbol{\Sigma}_{11}(\boldsymbol{\beta}_0))$ , where  $\boldsymbol{\Sigma}_{11} = \sum_{k=1}^K \pi_k \boldsymbol{\Sigma}_{11k}$ . Furthermore, let  $H_{11k}$  be the first  $s \times s$  submatrix of  $H_k$  and  $-\frac{1}{n_k} H_{11k} \rightarrow \boldsymbol{\Omega}_{11k}(\boldsymbol{\beta}_0)$  in probability, where  $\boldsymbol{\Omega}_{11k}$  is the first  $s \times s$  submatrix of  $\boldsymbol{\Omega}_k$ . Let  $\mathbf{b}_1$  be the first  $s$  elements of  $\mathbf{b}$ , and  $\mathbf{P}_{11}$  be the first  $s \times s$  submatrix of  $\mathbf{P}$ . By Slutsky's Theorem,

$$n^{1/2} \sum_{k=1}^K \pi_k (\boldsymbol{\Omega}_{11k} + \mathbf{P}_{11}) \{ \tilde{\boldsymbol{\beta}}_{r1}^S - \boldsymbol{\beta}_{01} + (\boldsymbol{\Omega}_{11k} + \mathbf{P}_{11k})^{-1} \mathbf{b}_1 \} \rightarrow N(\mathbf{0}, \boldsymbol{\Sigma}_{11}(\boldsymbol{\beta}_0)) \quad (36)$$

This completes the proof.

## A.2 The highly stratified PSH Model

Theorem 2 states selection consistency and the oracle properties of the penalization methods for the highly stratified PSH model.

**Theorem 2.** *For highly stratified data with finite  $n_k$ , when  $n \rightarrow \infty$ ,  $K \rightarrow \infty$ . The following holds under Condition A.1 - A.5,*

- (a.)  $\tilde{\boldsymbol{\beta}}_h^S$  is a root- $n$  consistent estimator for  $\boldsymbol{\beta}_0$ , i.e.  $\|\tilde{\boldsymbol{\beta}}_h^S - \boldsymbol{\beta}_0\| = O_p(n^{-1/2})$ .
- (b.) (Oracle properties) With probability tending to 1, the root- $n$  consistent estimator  $\tilde{\boldsymbol{\beta}}_h^S$  satisfies

- (i.) (Sparsity)  $\tilde{\boldsymbol{\beta}}_{2h}^S = \mathbf{0}$
- (ii.) (Asymptotic normality)  $n^{1/2}(\boldsymbol{\Omega}_{11} + \mathbf{P})\{\tilde{\boldsymbol{\beta}}_{1h}^S - \boldsymbol{\beta}_{01} + (\boldsymbol{\Omega}_{11} + \mathbf{P})^{-1} \mathbf{b}\} \rightarrow N(\mathbf{0}, \bar{\mathbf{m}}^{-1} \boldsymbol{\Sigma}_{11}(\boldsymbol{\beta}_0))$ , where  $\bar{\mathbf{m}} = \lim_{K \rightarrow \infty} n/K$ ,  $\boldsymbol{\Omega}_{11}$  and  $\boldsymbol{\Sigma}_{11}$  are the first  $s \times s$  submatrix of  $\boldsymbol{\Omega}(\boldsymbol{\beta}_0)$  and  $\boldsymbol{\Sigma}(\boldsymbol{\beta}_0)$ , defined in the Appendix.

Following the proof of Theorem 1, we briefly give the proof of Theorem 2.

### A.2.1 Proof of Theorem 2.a.

When data are highly-stratified, the strata size  $n_k$  is finite and  $K \rightarrow \infty$  as  $n \rightarrow \infty$ . To prove the validity of equation (13), we also write  $D_n(\mathbf{u}) = \frac{1}{n} \{Q^S(\boldsymbol{\beta}_0 + \alpha_n \mathbf{u}) - Q^S(\boldsymbol{\beta}_0)\}$ , and

$$D_n(\mathbf{u}) \leq \frac{1}{n} \sum_{k=1}^K \{l_k(\boldsymbol{\beta}_0 + \alpha_n \mathbf{u}) - l_k(\boldsymbol{\beta}_0)\} - \sum_{j=1}^s \{p_{\lambda_n}(|\beta_{j0} + \alpha_n u_j|) - p_{\lambda_n}(|\beta_{j0}|)\} \quad (37)$$

$$:= I_1 + I_2 \quad (38)$$

By Taylor expansion,

$$I_1 = \frac{1}{n} \sum_{k=1}^K \left( \frac{\partial l_k(\boldsymbol{\beta}_0)}{\partial \boldsymbol{\beta}} \right)^T \alpha_n \mathbf{u} - \frac{1}{2} \mathbf{u}^T \left\{ -\frac{1}{n} \sum_{k=1}^K \frac{\partial^2 l_k(\boldsymbol{\beta}_0)}{\partial \boldsymbol{\beta}^T \partial \boldsymbol{\beta}} + o_p(1) \right\} \mathbf{u} \alpha_n^2 \quad (39)$$

$$= O_p(\bar{m}^{-1/2} \alpha_n C) + O_p(\alpha_n^2 C^2) \quad (40)$$

where  $\bar{m} = n/K$  is the average strata size as  $n \rightarrow \infty$  and is a finite number. From Section A.1.1, term  $I_2$  has the order of  $C\alpha_n^2$  if  $b_n \rightarrow 0$ . By choosing a sufficiently large  $C$ ,  $O_p(C^2\alpha_n^2)$  dominates the others. Thus inequality(13) holds.

### A.2.2 Proof of Theorem 2.b. (i)

Following Section A.1.2, we prove equation (21) also holds when data are highly stratified. Based on the results from Zhou et al. (2001), the following holds

$$\frac{1}{K} \{l^S(\boldsymbol{\beta}) - l^S(\boldsymbol{\beta}_0)\} = \frac{1}{K} \sum_{k=1}^K \left[ \sum_{i=1}^{n_k} \int_0^\infty (\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \mathbf{Z}_{ki} dN_{ki}(u) - \int_0^\infty \log \frac{S_k^{(0)}(\boldsymbol{\beta}, u)}{S_k^{(0)}(\boldsymbol{\beta}_0, u)} d\bar{N}_k(u) \right] + o_p(1) \quad (41)$$

$$= \frac{1}{K} \sum_{k=1}^K X_k(\boldsymbol{\beta}) + o_p(1) \quad (42)$$

where  $S_k^{(p)}(\boldsymbol{\beta}, u) = \frac{1}{n_k} \sum_{i=1}^{n_k} w_{ik}(u) Y_{ik}(u) \mathbf{Z}_{ik}(u)^{\otimes p} \exp\{\boldsymbol{\beta}^T \mathbf{Z}_{ik}\}$  and  $d\bar{N}_k(u) = \sum_{i=1}^{n_k} dN_{ki}(u)$ .

Correspondingly,

$$X_k(\boldsymbol{\beta}) = \sum_{i=1}^{n_k} \int_0^\infty (\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \mathbf{Z}_{ki} dN_{ki}(u) - \int_0^\infty \log \frac{S_k^{(0)}(\boldsymbol{\beta}, u)}{S_k^{(0)}(\boldsymbol{\beta}_0, u)} d\bar{N}_k(u), \quad (43)$$

$$\chi_k(\boldsymbol{\beta}) = E\{X_k(\boldsymbol{\beta})\}, \text{ and } \chi(\boldsymbol{\beta}) = \lim_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \chi_k(\boldsymbol{\beta}) \quad (44)$$

$$\chi(\boldsymbol{\beta}_0) = 0, \quad \frac{\partial \chi(\boldsymbol{\beta}_0)}{\partial \boldsymbol{\beta}} = 0, \quad -\frac{\partial^2 \chi(\boldsymbol{\beta}_0)}{\partial \boldsymbol{\beta} \partial \boldsymbol{\beta}^T} = \mathbf{I}(\boldsymbol{\beta}_0) \quad (45)$$

Because  $\frac{1}{K} \sum_{k=1}^K E\{|X_k(\boldsymbol{\beta}) - \chi_k(\boldsymbol{\beta})|^2\} = O_p(1)$ , we obtain  $\frac{1}{K} \{l^S(\boldsymbol{\beta}) - l^S(\boldsymbol{\beta}_0)\} = \chi(\boldsymbol{\beta}) + O_p(K^{-1/2})$ . Also We also have  $\chi(\boldsymbol{\beta}) = -\frac{1}{2}(\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \{\mathbf{I}(\boldsymbol{\beta}_0) + o(1)\}(\boldsymbol{\beta} - \boldsymbol{\beta}_0)$ . By Taylor expansion, we obtain

$$\frac{\partial Q^S(\boldsymbol{\beta})}{\partial \beta_j} = \frac{\partial l^S(\boldsymbol{\beta})}{\partial \beta_j} - np'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j) \quad (46)$$

$$= K \sum_{l=1}^d \frac{\partial^2 \chi(\boldsymbol{\beta}_0)}{\partial \beta_j \partial \beta_l} (\beta_l - \beta_{l0}) + O_p(K^{1/2}) - np'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j) \quad (47)$$

$$= O_p(Kn^{-1/2} + K^{1/2}) - np'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j) \quad (48)$$

$$= K^{1/2} \{O_p(\bar{m}^{-1/2}) - \bar{m} K^{1/2} p'_{\lambda_n}(|\beta_j|) \text{sgn}(\beta_j)\} \quad (49)$$

As  $\lim_{K \rightarrow \infty} \bar{m} K^{1/2} \inf_{\|\beta\| \leq C n^{-1/2}} p'_{\lambda_n}(|\beta|) \rightarrow \infty$  in condition A5, the sign of  $\frac{\partial Q^S(\beta)}{\beta_j}$  is completely determined by the sign of  $\beta_j$ .

### A.2.3 Proof of Theorem 2.b. (ii)

There exists  $\tilde{\beta}_{h1}^S$  satisfying equation  $\frac{\partial Q(\beta)}{\partial \beta_1} \Big|_{\beta = ((\tilde{\beta}_{h1}^S)^T, \mathbf{0})^T} = 0$ . For  $j = 1, \dots, s$

$$\begin{aligned} 0 &= \frac{\partial l^S(\beta)}{\partial \beta_j} \Big|_{\beta = ((\tilde{\beta}_{h1}^S)^T, \mathbf{0})^T} - n p'_{\lambda_n}(|\tilde{\beta}_j|) \text{sgn}(\tilde{\beta}_{hj}^S) \\ &= \frac{\partial l^S(\beta_0)}{\partial \beta_j} - \sum_{l=1}^s \left\{ -\frac{\partial^2 l^S(\beta_0)}{\partial \beta_j \partial \beta_l} \right\} (\tilde{\beta}_{hl}^S - \beta_{l0}) - n \left( p'_{\lambda_n}(|\beta_{j0}|) \text{sgn}(\beta_{j0}) + \{p''_{\lambda_n}(|\beta_{j0}|) + o_p(1)\} (\tilde{\beta}_{hj}^S - \beta_{j0}) \right) \end{aligned} \quad (50)$$

Denote  $U_h^S(\beta)$  and  $H_h^S(\beta)$  as the score function and the Hessian matrix for highly stratified data. The sub-vector  $U_{h1}^S(\beta)$  is the first element of  $U_h^S(\beta)$ , and  $H_{h11}^S(\beta)$  is the first  $s \times s$  matrix of  $H_h^S(\beta)$ . As  $K \rightarrow \infty$ ,  $K^{-1/2} U_{h1}^S(\beta_0) \rightarrow N(\mathbf{0}, \Sigma_{11h}(\beta_0))$  in distribution, where  $\Sigma_{11h}$  is the first  $s \times s$  submatrix of  $\Sigma_h$ . Details of the matrix  $\Sigma_h$  can be found in Zhou et al.(2011). Also  $-\frac{1}{n} H_{h11} \rightarrow \Omega_{h11}(\beta_0)$  in probability, and  $\Omega_{h11}$  is the first  $s \times s$  submatrix of  $\Omega_h$ . Here  $\bar{m} \Omega_h$  equals to  $\mathbf{I}$  defined in condition A3. By Slutsky's Theorem,

$$n^{1/2}(\Omega_{11} + \mathbf{P}_{11})\{\tilde{\beta}_1 - \beta_{01} + (\Omega_{11} + \mathbf{P}_{11})^{-1} \mathbf{b}_1\} \rightarrow N(\mathbf{0}, \bar{m}^{-1} \Sigma_{11}(\beta_0)) \quad (51)$$

This completes the proof.

## A.3 Oracle Properties of Penalties

Conditions A.4 and A.5 provide guidance to select penalties that will have the oracle properties in the stratified PSH model. With a proper choice of  $\lambda$ , we show that ALASSO, SCAD, and MCP satisfy the two conditions.

- (a). ALASSO: since Zhou et al. (2011) have shown that  $\hat{\beta}$  is root- $n$  consistent, the data-adaptive weight  $\theta_j = |\hat{\beta}_j^S|^{-1}$  has the order of  $n^{1/2}$ . When  $\sqrt{n} \lambda_n \rightarrow 0$ ,  $\sqrt{n} a_n = \sqrt{n} \lambda_n \theta \rightarrow 0$  and  $b_n = 0$ . Hence Condition A.4 is satisfied. For regularly stratified data, when  $n_k \lambda_n \rightarrow \infty$ ,  $\lim_{n_k \rightarrow \infty} \sqrt{n_k} \inf_{\|\beta\| \leq C n^{-1/2}} p'_{\lambda_n}(|\beta|) = \sqrt{n_k} \lambda_n \theta = n_k \pi_k^{1/2} \lambda_n \rightarrow \infty$ . For highly stratified data, when  $K \lambda_n \rightarrow \infty$ ,  $\lim_{K \rightarrow \infty} \bar{m} K^{1/2} \inf_{\|\beta\| \leq C n^{-1/2}} p'_{\lambda_n}(|\beta|) = \bar{m}^{3/2} K \lambda_n \rightarrow \infty$ . Condition A.5 is satisfied.
- (b). SCAD: when  $\lambda_n \rightarrow 0$ ,  $a_n = b_n = 0$ . Condition A.4 is satisfied. For regular stratified data, When  $\sqrt{n_k} \lambda_n \rightarrow \infty$ ,  $\lim_{n_k \rightarrow \infty} \sqrt{n_k} \inf_{\|\beta\| \leq C n^{-1/2}} p'_{\lambda_n}(|\beta|) = \sqrt{n_k} \lambda_n \rightarrow \infty$ ; for highly-stratified data, when  $K^{1/2} \lambda_n \rightarrow \infty$ ,  $\lim_{K \rightarrow \infty} \bar{m} K^{1/2} \inf_{\|\beta\| \leq C n^{-1/2}} p'_{\lambda_n}(|\beta|) = \bar{m} K^{1/2} \lambda_n \rightarrow \infty$ . Condition A.5 holds.

- (c). MCP: when  $\lambda_n \rightarrow 0$ ,  $a_n = b_n = 0$  for sufficiently large  $n$ . Condition A.4 is satisfied. For regularly stratified data, when  $\sqrt{n_k}\lambda_n \rightarrow \infty$ ,  $\sqrt{n_k} \inf_{\|\beta\| \leq Cn^{-1/2}} p'_{\lambda_n}(|\beta|) = \sqrt{n_k}\lambda_n - C\sqrt{\pi_k}/\gamma \rightarrow \infty$ . For highly stratified data, when  $K^{1/2}\lambda_n \rightarrow \infty$ ,  $\bar{m}K^{1/2} \inf_{\|\beta\| \leq Cn^{-1/2}} p'_{\lambda_n}(|\beta|) = \bar{m}K^{1/2}\lambda_n - C\bar{m}^{1/2}/\gamma \rightarrow \infty$ . Condition A.5 holds.

Hence, according to Theorem 1 and Theorem 2, when  $\lambda_n$  is chosen appropriately, the three penalized estimators possess the oracle properties under both stratification regimes and asymptotically follow a normal distribution  $\sqrt{n}(\tilde{\beta}_{1r}^S - \beta_{01}) \rightarrow N(\mathbf{0}, (\sum_{k=1}^K \pi_k \mathbf{\Omega}_{11k})^{-1} (\sum_{k=1}^K \pi_k \mathbf{\Sigma}_{11k}) (\sum_{k=1}^K \pi_k \mathbf{\Omega}_{11k})^{-1})$  when data are regularly stratified, and follow  $\sqrt{n}(\tilde{\beta}_{1h}^S - \beta_{01}) \rightarrow N(\mathbf{0}, \mathbf{\Omega}_{11}^{-1} \bar{m}^{-1} \mathbf{\Sigma}_{11} \mathbf{\Omega}_{11}^{-1})$  when data are highly stratified.

For LASSO, the oracle properties do not hold. From Condition A.4,  $a_n = \lambda_n = O_p(n^{-1/2})$  and  $b_n = 0$ , whereas Condition A.5 requires that  $n_k^{1/2}\lambda_n = \pi_k^{1/2}n^{1/2}\lambda \rightarrow \infty$  for regularly stratified data and  $\bar{m}^{1/2}n^{1/2}\lambda_n \rightarrow \infty$  for highly stratified data. The two conditions can not be simultaneously held.

## Appendix B Large Sample Properties of the Penalized Marginal PSH Model

We assume the following regularity conditions

B1.  $\int_0^\tau \lambda_{10}(t)dt < \infty$

B2. Define

$$\mathbf{s}^{(p)}(\beta, t) = \lim_{K \rightarrow \infty} K^{-1} \sum_{k=1}^K \sum_{i=1}^{n_k} I(C_{ki} \geq t) Y_{ki}(t) Z_{ki}^{\otimes p} \exp(\beta^T \mathbf{Z}_{ki}) \quad (52)$$

$$\mathbf{S}^{(p)}(\beta, t) = K^{-1} \sum_{k=1}^K \sum_{i=1}^{n_k} I(C_{ki} \geq t) Y_{ki}(t) Z_{ki}^{\otimes p} \exp(\beta^T \mathbf{Z}_{ki}) \quad (53)$$

$$\hat{\mathbf{S}}^{(p)}(\beta, t) = K^{-1} \sum_{k=1}^K \sum_{i=1}^{n_k} \hat{w}_{ki}(t) Y_{ki}(t) Z_{ki}^{\otimes p} \exp(\beta^T \mathbf{Z}_{ki}) \quad (54)$$

There exists a neighborhood  $\mathcal{B}$  of  $\beta_0$  such that the following conditions are satisfied: (i) there exists a scalar, a vector, and a matrix function  $s^{(0)}$ ,  $\mathbf{s}^{(1)}$ , and  $\mathbf{s}^{(2)}$  defined on  $\mathcal{B} \times [0, \tau]$  such that  $\sup_{t \in [0, \tau], \beta \in \mathcal{B}} \|\mathbf{S}^{(p)}(\beta, t) - \mathbf{s}^{(p)}(\beta, t)\| \rightarrow 0$  in probability,  $p = 0, 1, 2$ ; (ii). the matrix  $\mathbf{\Omega}^M = \int_0^\tau \mathbf{v}(\beta_0, t) s^{(0)}(\beta_0, t) \lambda_{10}(t) dt$  is positive definite, where  $\mathbf{v} = \mathbf{s}^{(2)}/s^{(0)} - (\mathbf{s}^{(1)}/s^{(0)})(\mathbf{s}^{(1)}/s^{(0)})^T$ .

B3.  $\mathbf{s}^{(p)}(\beta, t)$  are continuous functions of  $\beta \in \mathcal{B}$  uniformly in  $t \in [0, \tau]$  and are bounded on  $\mathcal{B} \times [0, \tau]$ ,  $s^{(0)}(\beta, t)$  is bounded away from zero.

B4. The penalty function satisfies that  $a_K = O_p(K^{-1/2})$  and  $b_K \rightarrow 0$ .



B5.  $p_{\lambda_n}(|\beta|)$  satisfies  $\lim_{K \rightarrow \infty} K^{1/2} \inf_{|\beta| \leq CK^{-1/2}} p'_{\lambda_K}(|\beta|) \rightarrow \infty$ .

The following theorem states selection consistency and the oracle properties of the penalization methods for the marginal PSH model.

**Theorem 3.** *Under Condition B.1 - B.4 in the Appendix, the following holds as  $K \rightarrow \infty$ ,*

- a.  $\tilde{\beta}^M$  is a root- $K$  consistent estimator for  $\beta_0$ , i.e.  $\|\tilde{\beta}^M - \beta_0\| = O_p(K^{-1/2})$ .
- b. (Oracle properties) With probability tending to 1, the root- $K$  consistent estimator  $\tilde{\beta}$  satisfies
  - i. (Sparsity)  $\tilde{\beta}_2^M = \mathbf{0}$
  - ii. (Asymptotic normality)  $K^{1/2}(\Omega_{11}^M + \mathbf{P}_{11})\{\tilde{\beta}_1^M - \beta_{01} + (\Omega_{11}^M + \mathbf{P}_{11})^{-1}\mathbf{b}_1\} \rightarrow N(\mathbf{0}, \Sigma_{11}^M(\beta_0))$ , where  $\Omega_{11}^M$  and  $\Sigma_{11}^M$  are the first  $s \times s$  submatrix of  $\Omega^M(\beta_0)$  and  $\Sigma^M(\beta_0)$ , defined in the Appendix.

## B.1 Proof of Theorem 3.a.

It is sufficient to prove that for any positive  $\epsilon$ , there exists a large constant  $C$  such that

$$Pr\left\{\sup_{\|\mathbf{u}\|=C} Q^M(\beta_0 + \alpha_K \mathbf{u}) < Q^M(\beta_0)\right\} \geq 1 - \epsilon \quad (55)$$

where  $\alpha_K = K^{-1/2} + a_K$ . Denote  $D_K(\mathbf{u}) = \frac{1}{K}\{Q^C(\beta_0 + \alpha_K \mathbf{u}) - Q^C(\beta_0)\}$ , and

$$D_K(\mathbf{u}) \leq \frac{1}{K}l^M(\beta_0 + \alpha_K \mathbf{u}) - l^M(\beta_0) - \sum_{j=1}^s \{p_{\lambda_K}(|\beta_{j0} + \alpha_K u_j|) - p_{\lambda_K}(|\beta_{j0}|)\} \quad (56)$$

By Taylor expansion, the first part

$$I_1 = \frac{1}{K} \left( \frac{\partial l^M(\beta_0)}{\partial \beta} \right)^T \alpha_K \mathbf{u} - \frac{1}{2} \mathbf{u}^T \left\{ -\frac{1}{K} \frac{\partial^2 l^M(\beta_0)}{\partial \beta^T \partial \beta} + o_p(1) \right\} \mathbf{u} \alpha_K^2 \quad (57)$$

$$= O_p(\alpha_K^2 C) + O_p(\alpha_K^2 C^2) \quad (58)$$

From Section A.1.1, term  $I_2$  has the order of  $C\alpha_K^2$  if  $b_K \rightarrow 0$ . By choosing a sufficiently large  $C$ ,  $O_p(C^2\alpha_K^2)$  dominates the others. Thus inequality(55) holds.

## B.2 Proof of Theorem 3.b.(i)

Define the following process

$$X(\boldsymbol{\beta}, \tau) = \frac{1}{K} \{l^M(\boldsymbol{\beta}) - l^M(\boldsymbol{\beta}_0)\} \quad (59)$$

$$= \frac{1}{K} \sum_{k=1}^K \sum_{i=1}^{n_k} \int_0^\tau \{(\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \mathbf{Z}_{ki} - \log \frac{\hat{S}^{(0)}(\boldsymbol{\beta}, u)}{\hat{S}^{(0)}(\boldsymbol{\beta}_0, u)}\} \hat{w}_{ki}(u) dN_{ki}(u) \quad (60)$$

$$A(\boldsymbol{\beta}, \tau) = \frac{1}{K} \sum_{k=1}^K \sum_{i=1}^{n_k} \int_0^\tau \{(\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \mathbf{Z}_{ki} - \log \frac{\hat{S}^{(0)}(\boldsymbol{\beta}, u)}{\hat{S}^{(0)}(\boldsymbol{\beta}_0, u)}\} \hat{w}_{ki}(u) \lambda_1(u) du \quad (61)$$

$$= \int_0^\tau \{(\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \hat{\mathbf{S}}^{(1)}(\boldsymbol{\beta}_0, u) - \hat{S}^{(0)}(\boldsymbol{\beta}_0, u) \log \frac{\hat{S}^{(0)}(\boldsymbol{\beta}, u)}{\hat{S}^{(0)}(\boldsymbol{\beta}_0, u)}\} \lambda_{10}(u) du \quad (62)$$

From Zhou et al (2012), we have  $X(\boldsymbol{\beta}, \cdot) - A(\boldsymbol{\beta}, \cdot) \rightarrow 0$  in probability and  $\lim_{K \rightarrow \infty} \hat{\mathbf{S}}^{(p)}(\boldsymbol{\beta}, t) = G(t) \mathbf{s}^{(p)}(\boldsymbol{\beta}, t)$ . Thus for each  $\boldsymbol{\beta} \in \mathcal{B}$ ,

$$A(\boldsymbol{\beta}, \tau) \rightarrow f(\boldsymbol{\beta}, \tau) = \int_0^\tau \{(\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \mathbf{s}^{(1)}(\boldsymbol{\beta}_0, u) - s^{(0)}(\boldsymbol{\beta}_0, u) \log \frac{s^{(0)}(\boldsymbol{\beta}, u)}{s^{(0)}(\boldsymbol{\beta}_0, u)}\} \lambda_{10}(u) du \quad (63)$$

where  $f$  has the following properties

$$f(\boldsymbol{\beta}_0) = 0, \quad \frac{\partial f(\boldsymbol{\beta}_0)}{\partial \boldsymbol{\beta}} = 0, \quad -\frac{\partial^2 f(\boldsymbol{\beta}_0)}{\partial \boldsymbol{\beta} \partial \boldsymbol{\beta}^T} = \boldsymbol{\Omega}^M(\boldsymbol{\beta}_0) \quad (64)$$

Then the following holds

$$\frac{1}{K} \{l^M(\boldsymbol{\beta}) - l^M(\boldsymbol{\beta}_0)\} = f(\boldsymbol{\beta}, \tau) + O_p\left(\frac{\|\boldsymbol{\beta} - \boldsymbol{\beta}_0\|}{\sqrt{K}}\right) \quad (65)$$

We also have  $f(\boldsymbol{\beta}) = -\frac{1}{2}(\boldsymbol{\beta} - \boldsymbol{\beta}_0)^T \{\boldsymbol{\Omega}(\boldsymbol{\beta}_0) + o_p(1)\}(\boldsymbol{\beta} - \boldsymbol{\beta}_0)$ . By Taylor expansion, we obtain

$$\frac{\partial Q^M(\boldsymbol{\beta})}{\partial \beta_j} = \frac{\partial l^M(\boldsymbol{\beta})}{\partial \beta_j} - K p'_{\lambda_K}(|\beta_j|) \text{sgn}(\beta_j) \quad (66)$$

$$= K \sum_{l=1}^d \frac{\partial^2 f(\boldsymbol{\beta}_0)}{\partial \beta_j \partial \beta_l} (\beta_l - \beta_{l0}) + O_p(K^{1/2} \|\boldsymbol{\beta} - \boldsymbol{\beta}_0\|) - K p'_{\lambda_K}(|\beta_j|) \text{sgn}(\beta_j) \quad (67)$$

$$= O_p(K^{1/2}) + O_p(1) - K p'_{\lambda_K}(|\beta_j|) \text{sgn}(\beta_j) \quad (68)$$

$$= K^{1/2} \{O_p(1) - K^{1/2} p'_{\lambda_K}(|\beta_j|) \text{sgn}(\beta_j)\} \quad (69)$$

Since  $\lim_{K \rightarrow \infty} K^{1/2} \inf_{\|\boldsymbol{\beta}\| \leq CK^{-1/2}} p'_{\lambda_K}(|\beta|) \rightarrow \infty, k = 1, \dots, K$ , the sign of  $\frac{\partial Q^C(\boldsymbol{\beta})}{\beta_j}$  is completely determined by the sign of  $\beta_j$ .

### B.3 Proof of Theorem 3.b. (ii)

It is easy to show that there exists a root-n consistent local maximizer  $\tilde{\beta}_1$  of  $Q(\beta_1, \mathbf{0})$ , satisfying equation

$\frac{\partial Q^M(\beta)}{\partial \beta_1} \Big|_{\beta=(\tilde{\beta}_1^T, \mathbf{0})^T} = 0$ . Denote  $U^M(\beta)$  and  $H^M(\beta)$  as the score function and the Hessian matrix of  $l^M(\beta)$  and it is

$$U^M(\beta) = \sum_{k=1}^K \sum_{i=1}^{n_k} \int_0^\infty \left\{ \mathbf{Z}_{ik} - \frac{\hat{\mathbf{S}}^{(1)}(\beta, u)}{\hat{S}^{(0)}(\beta, u)} \right\} \hat{w}_{ik}(u) dN_{ik}(u) \quad (70)$$

$$H^M(\beta) = \sum_{k=1}^K \sum_{i=1}^{n_k} \int_0^\infty \left[ \frac{\hat{\mathbf{S}}^{(2)}(\beta, u)}{\hat{S}^{(0)}(\beta, u)} - \left\{ \frac{\hat{\mathbf{S}}^{(1)}(\beta, u)}{\hat{S}^{(0)}(\beta, u)} \right\}^{\otimes 2} \right] \hat{w}_{ik}(u) dN_{ik}(u) \quad (71)$$

For  $j = 1, \dots, s$

$$\begin{aligned} 0 &= \frac{\partial l^M(\beta)}{\partial \beta_j} \Big|_{\beta=(\tilde{\beta}_1^T, \mathbf{0})^T} - K p'_{\lambda_n}(|\tilde{\beta}_j|) \text{sgn}(\tilde{\beta}_j) \\ &= \frac{\partial l^M(\beta_0)}{\partial \beta_j} - \sum_{l=1}^s \left\{ -\frac{\partial^2 f(\beta_0)}{\partial \beta_j \partial \beta_l} + o_p(1) \right\} (\tilde{\beta}_l - \beta_{l0}) - \\ &\quad K \left( p'_{\lambda_K}(|\beta_{j0}|) \text{sgn}(\beta_{j0}) + \{p''_{\lambda_K}(|\beta_{j0}|) + o_p(1)\} (\tilde{\beta}_j - \beta_{j0}) \right) \end{aligned} \quad (72)$$

Denote  $U_{11}^M(\beta)$  as the first  $s$  elements of the score function  $U^M(\beta)$ . As  $K \rightarrow \infty$ ,  $K^{-1/2} U_{11}^M(\beta_0) \rightarrow N(\mathbf{0}, \Sigma_{11}^M(\beta_0))$  in distribution, where  $\Sigma_{11}^M$  is the first  $s \times s$  submatrix of  $\Sigma^M$ . Furthermore, let  $H_{11}^M$  be the first  $s \times s$  submatrix of  $H^M$  and  $-\frac{1}{K} H_{11}^M \rightarrow \Omega_{11}^M(\beta_0)$  in probability, where  $\Omega_{11}^M$  is the first  $s \times s$  submatrix of  $\Omega^M$ . Let  $\mathbf{b}_1$  be the first  $s$  elements of  $\mathbf{b}$ , and  $\mathbf{P}_{11}$  be the first  $s \times s$  submatrix of  $\mathbf{P}$ . By Slutsky's Theorem,

$$K^{1/2}(\Omega_{11}^M + \mathbf{P}_{11})\{\tilde{\beta}_1 - \beta_{01} + (\Omega_{11}^M + \mathbf{P}_{11})^{-1} \mathbf{b}_1\} \rightarrow N(\mathbf{0}, \Sigma_{11}^M(\beta_0)) \quad (73)$$

This completes the proof.

To achieve the oracle properties, penalty functions need satisfy Condition B.3 – B.4. Borrowing the arguments in Section (A.3), we can easily show that the oracle properties of ALASSO, SCAD, and MCP hold when  $\lambda$  is chosen appropriately: (a). ALASSO possesses the oracle properties when  $\sqrt{K}\lambda_K \rightarrow 0$ ,  $K\lambda_K \rightarrow \infty$ , and  $\theta_j = |\hat{\beta}_j^M|^{-1}$ , where  $|\hat{\beta}_j^M|^{-1}$  is the maximizer of the pseudopartial likelihood with root- $K$  consistency; (b). SCAD and MCP have the oracle properties when  $\lambda_K \rightarrow 0$  and  $\sqrt{K}\lambda_K \rightarrow \infty$ ; (c). the oracle properties do not hold for LASSO.

## Appendix C Complete Selection Results in the UNOS Data Analysis

Table 8: Complete Variable selection results and estimated regression coefficients using UNOS data.

	KDRI	LASSO	Regularly Stratified		MCP	LASSO	Highly Stratified		MCP	LASSO	Marginal		MCP
	ALASSO	SCAD				ALASSO	SCAD			ALASSO	SCAD		
<b>Donor Factors</b>													
Age -40 yrs (applies to all ages)	0.013(0.002)	0.012(0.001)	0.013(0.001)	0.013(0.001)	0.012(0.001)	0.011(0.001)	0.013(0.001)	0.013(0.001)	0.012(0.001)	0.012(0.001)	0.013(0.001)	0.012(0.001)	0.012(0.001)
Age -18 yrs (applies only if age<18)	-0.019(0.010)	-0.01(0.008)	-0.013(0.006)	-0.005(0.007)	-0.005(0.007)	-0.015(0.006)	-0.014(0.005)	-0.005(0.005)	-0.005(0.005)	-0.014(0.008)	-0.018(0.007)	-0.014(0.008)	-0.014(0.008)
Age -50 yrs (applies only if age>50)	0.011(0.006)	0.020(0.003)	0.018(0.003)	0.018(0.003)	0.019(0.003)	0.018(0.003)	0.016(0.002)	0.018(0.002)	0.019(0.002)	0.020(0.003)	0.018(0.003)	0.020(0.003)	0.020(0.003)
African American race	0.179(0.071)	0.170(0.031)	0.167(0.031)	0.172(0.031)	0.168(0.031)	0.151(0.023)	0.148(0.027)	0.174(0.026)	0.169(0.027)	0.164(0.033)	0.157(0.033)	0.166(0.033)	0.166(0.033)
Male	-	-0.037(0.026)	-	-	-	-0.042(0.018)	-	-	-	-0.035(0.026)	-0.027(0.023)	-0.034(0.026)	-0.034(0.026)
Height: per 10 cm increase	-0.046(0.015)	-0.021(0.013)	-	-0.031(0.011)	-0.029(0.011)	-0.008(0.01)	-	-0.031(0.008)	-0.028(0.009)	-0.018(0.014)	-	-0.019(0.014)	-0.019(0.014)
Weight (per 5 kg increase if <80 kg)	-0.020(0.010)	-0.227(0.06)	-0.311(0.052)	-0.248(0.059)	-0.241(0.059)	-0.169(0.048)	-0.215(0.043)	-0.251(0.05)	-0.244(0.045)	-0.213(0.064)	-0.235(0.059)	-0.220(0.064)	-0.220(0.064)
Donation after cardiac death	0.133(0.132)	-	-	-	-	-	-	-	-	-	-	-	-
Cause of death: stroke	0.088(0.051)	0.061(0.025)	0.073(0.024)	-	0.067(0.024)	0.067(0.021)	0.040(0.019)	-	0.069(0.022)	0.066(0.025)	0.053(0.025)	0.066(0.025)	0.066(0.025)
Serum creatinine-1 (applies to all Cr values )	0.220(0.051)	0.195(0.036)	0.174(0.035)	0.183(0.035)	0.186(0.035)	0.150(0.026)	0.107(0.028)	0.183(0.022)	0.187(0.029)	0.192(0.035)	0.155(0.035)	0.196(0.035)	0.196(0.035)
Serum creatinine-1 (applies if Cr>1.5 )	-0.209(0.082)	-0.189(0.05)	-0.165(0.049)	-0.176(0.049)	-0.179(0.049)	-0.143(0.034)	-0.099(0.036)	-0.177(0.032)	-0.18(0.036)	-0.185(0.046)	-0.148(0.046)	-0.189(0.046)	-0.189(0.046)
Diabetic	0.130(0.076)	0.233(0.047)	0.237(0.047)	0.228(0.047)	0.232(0.047)	0.212(0.039)	0.191(0.038)	0.231(0.034)	0.235(0.036)	0.242(0.05)	0.229(0.049)	0.245(0.05)	0.245(0.05)
Hypertensive	0.126(0.102)	0.137(0.026)	0.139(0.026)	0.151(0.026)	0.138(0.026)	0.132(0.02)	0.130(0.021)	0.15(0.018)	0.136(0.022)	0.142(0.027)	0.143(0.027)	0.142(0.027)	0.142(0.027)
Cigarette users	-	0.027(0.021)	-	-	-	0.017(0.013)	-	-	-	0.024(0.018)	-	0.025(0.018)	0.025(0.018)
Positive HCV status	0.240(0.153)	0.098(0.068)	-	-	-	0.070(0.048)	-	-	-	0.133(0.064)	0.055(0.064)	0.135(0.064)	0.135(0.064)
<b>Transplant Factors</b>													
Cold ischemic time ( per 1 hr (ref=20 hr) )	0.005(0.003)	0.003(0.001)	-	-	-	0.002(0.001)	-	-	-	0.004(0.002)	0.002(0.001)	0.004(0.002)	0.004(0.002)
Organ sharing	-	-	-	-	-	-	-	-	-	-	-	-	-
Regional(ref=local)	-	0.061(0.037)	-	-	-	0.045(0.022)	-	-	-	0.030(0.038)	-	0.031(0.038)	0.031(0.038)
National(ref=local)	-	-0.052(0.031)	-	-	-	-0.038(0.027)	-	-	-	-0.049(0.037)	-	-0.051(0.037)	-0.051(0.037)
HLA-B mismatch 0 (ref=2 B MM)	-0.077(0.056)	-0.155(0.034)	-0.176(0.031)	-0.174(0.031)	-0.174(0.031)	-0.141(0.028)	-0.134(0.025)	-0.174(0.027)	-0.174(0.03)	-0.154(0.039)	-0.158(0.039)	-0.156(0.039)	-0.156(0.039)
1	-0.061(0.041)	-0.068(0.023)	-0.07(0.023)	-0.069(0.023)	-0.069(0.023)	-0.057(0.019)	-0.051(0.021)	-0.067(0.018)	-0.067(0.017)	-0.055(0.025)	-0.052(0.024)	-0.056(0.025)	-0.056(0.025)
HLA-DR mismatch 0 (ref=1 DR MM)	-0.130(0.041)	-0.097(0.027)	-0.103(0.027)	-0.102(0.027)	-0.102(0.027)	-0.087(0.024)	-0.078(0.02)	-0.102(0.024)	-0.102(0.023)	-0.091(0.03)	-0.084(0.029)	-0.092(0.03)	-0.092(0.03)
2	0.077(0.051)	0.055(0.023)	0.057(0.023)	0.058(0.023)	0.057(0.023)	0.051(0.018)	0.047(0.019)	0.058(0.017)	0.057(0.02)	0.063(0.025)	0.058(0.025)	0.063(0.025)	0.063(0.025)
Transplant year	-	-0.155(0.021)	-0.161(0.021)	-0.165(0.021)	-0.163(0.021)	-0.139(0.018)	-0.139(0.021)	-0.166(0.02)	-0.164(0.02)	-0.151(0.025)	-0.156(0.025)	-0.152(0.025)	-0.151(0.025)
En bloc transplant	-0.346(0.138)	-0.313(0.117)	-0.285(0.116)	-0.317(0.117)	-0.312(0.117)	-0.209(0.094)	-0.083(0.085)	-0.310(0.094)	-0.304(0.081)	-0.295(0.124)	-0.132(0.122)	-0.304(0.124)	-0.304(0.124)
Double kidney transplant	-0.148(0.22)	-0.334(0.093)	-0.329(0.092)	-0.332(0.092)	-0.33(0.092)	-0.247(0.063)	-0.181(0.047)	-0.331(0.067)	-0.330(0.061)	-0.329(0.078)	-0.250(0.078)	-0.338(0.078)	-0.338(0.078)
ABO identical	-	-	-	-	-	-	-	-	-	-0.023(0.052)	-	-0.026(0.052)	-0.027(0.052)
<b>Recipient Factors</b>													
Age	-	-0.025(0.001)	-0.025(0.001)	-0.025(0.001)	-0.025(0.001)	-0.024(0.001)	-0.025(0.001)	-0.025(0.001)	-0.025(0.001)	-0.025(0.001)	-0.025(0.001)	-0.025(0.001)	-0.025(0.001)
African America	-	0.356(0.025)	0.359(0.025)	0.363(0.024)	0.363(0.024)	0.362(0.02)	0.386(0.02)	0.364(0.02)	0.364(0.019)	0.372(0.027)	0.384(0.028)	0.371(0.027)	0.371(0.027)
Male	-	-0.049(0.022)	-0.053(0.022)	-	-	-0.032(0.017)	-0.018(0.015)	-	-	-0.06(0.026)	-0.039(0.021)	-0.063(0.026)	-0.063(0.026)
Primary diagnosis (ref=GN)													
Diabetes	-	-0.075(0.03)	-0.080(0.03)	-0.079(0.03)	-0.079(0.03)	-0.063(0.023)	-0.053(0.023)	-0.074(0.023)	-0.074(0.026)	-0.059(0.033)	-0.054(0.033)	-0.060(0.033)	-0.060(0.033)
Hypertension	-	0.102(0.029)	0.100(0.029)	0.098(0.029)	0.097(0.029)	0.088(0.02)	0.074(0.021)	0.101(0.019)	0.101(0.021)	0.119(0.028)	0.109(0.028)	0.121(0.028)	0.121(0.028)
Failed transplants	-	0.545(0.142)	0.546(0.142)	0.538(0.142)	0.539(0.142)	0.479(0.116)	0.432(0.096)	0.540(0.094)	0.542(0.109)	0.561(0.141)	0.522(0.141)	0.570(0.141)	0.570(0.141)
CAKUT/Congenital uropathy	-	-0.191(0.038)	-0.193(0.038)	-0.191(0.038)	-0.192(0.038)	-0.164(0.03)	-0.136(0.03)	-0.194(0.029)	-0.194(0.029)	-0.197(0.04)	-0.179(0.039)	-0.200(0.04)	-0.200(0.04)
Others	-	0.048(0.032)	0.051(0.032)	0.057(0.032)	0.057(0.032)	0.045(0.032)	0.044(0.025)	0.061(0.023)	0.061(0.027)	0.072(0.037)	0.072(0.037)	0.073(0.037)	0.073(0.037)
Blood transfusion	-	0.040(0.022)	-	-	-	0.034(0.017)	-	-	-	0.032(0.023)	-	0.033(0.023)	0.033(0.023)
Height	-	-	-	-	-	-	-	-	-	0.001(0.001)	-	0.001(0.001)	0.001(0.001)
Weight	-	0.005(0.001)	0.005(0.001)	0.005(0.001)	0.005(0.001)	0.004(0.0005)	0.004(0.001)	0.005(0.0005)	0.005(0.0005)	0.005(0.001)	0.005(0.001)	0.005(0.001)	0.005(0.001)
Peak PRA (ref=0)													
1-50	-	0.057(0.023)	0.057(0.023)	0.060(0.023)	0.061(0.023)	0.044(0.015)	0.029(0.019)	0.060(0.02)	0.061(0.017)	0.037(0.024)	0.031(0.024)	0.038(0.024)	0.038(0.024)
51-80	-	0.116(0.057)	0.119(0.057)	0.138(0.057)	0.137(0.057)	0.095(0.048)	0.066(0.047)	0.142(0.047)	0.141(0.048)	0.096(0.06)	0.081(0.06)	0.098(0.06)	0.098(0.06)
>80	-	0.244(0.048)	0.246(0.047)	0.268(0.047)	0.267(0.047)	0.196(0.035)	0.134(0.036)	0.269(0.037)	0.268(0.034)	0.231(0.049)	0.194(0.049)	0.236(0.049)	0.236(0.049)
Years of RRT (ref: <=1)													
2-3	-	-	-	-	-	-	-	-	-	-0.013(0.022)	-0.004(0.022)	-0.015(0.022)	-0.015(0.022)
>3	-	-	-	-	-	-	-	-	-	-0.031(0.028)	-0.010(0.027)	-0.035(0.028)	-0.035(0.028)
Angina pectoris	-	-0.059(0.035)	-	-	-	-0.041(0.026)	-	-	-	-0.048(0.035)	-0.034(0.035)	-0.050(0.035)	-0.050(0.035)
Peripheral vascular disease	-	-	-	-	-	-	-	-	-	-	-	-	-
COPD	-	-	-	-	-	-	-	-	-	-0.085(0.115)	-	-0.092(0.115)	-0.092(0.115)
Positive HCV status	-	0.207(0.044)	0.242(0.037)	0.237(0.037)	0.238(0.037)	0.196(0.035)	0.208(0.032)	0.237(0.026)	0.237(0.029)	0.195(0.043)	0.204(0.043)	0.197(0.043)	0.197(0.043)
Diabetic	-	-	-	-	-	-	-	-	-	-	-	-	-

HCV: Hepatitis C. Cr: serum creatinine. HLA: human leukocyte antigen. GN: glomerulonephritis CAKUT: congenital anomalies of the kidney and urinary tract. RRT: renal replacement therapy COPD: chronic obstructive pulmonary disease.

## Appendix D Simulations Results for Dependent Censoring

We consider three scenarios when censoring times and covariates are dependent. In Scenario (a), we allowed the censoring to depend on important variables  $z_1$  and  $z_4$ ; in Scenario (b), censoring times depend on non-important variables  $z_5$  and  $z_8$ ; in Scenario (c), censoring times depend on both important and non-important variables  $z_1$  and  $z_3$ ; in Scenario (d), we displayed the results when censoring and covariates are independent.

### D.1 Penalized Stratified PSH Model

#### D.1.1 Regularly Stratified

Table 9: Selection results of the penalized stratified based on 100 replications with different censoring patterns, where  $K = 3$ ,  $n = 200$ ,  $p = 0.6$ , the censoring rate is 28%, and the event rate is 45%

Scenario	Depend on	Penalty	C (5)	IC (0)	Pcorr	MMSE
(a)	$z_1, z_4$	MPLE	0	0	0%	0.137
		LASSO	3.43	0	20%	0.166
		ALASSO	4.73	0.02	76%	0.086
		SCAD	4.89	0.03	90%	0.053
		MCP	4.90	0.02	90%	0.052
		Oracle	5	0	100%	0.050
(b)	$z_5, z_8$	MPLE	0	0	0%	0.143
		LASSO	3.64	0.01	21%	0.125
		ALASSO	4.79	0.03	78%	0.084
		SCAD	4.89	0.02	87%	0.059
		MCP	4.92	0.02	90%	0.056
		Oracle	5	0	100%	0.051
(c)	$z_1, z_3$	MPLE	0	0	0%	0.134
		LASSO	3.54	0	23%	0.148
		ALASSO	4.79	0.02	81%	0.083
		SCAD	4.88	0.02	89%	0.056
		MCP	4.90	0.02	91%	0.054
		Oracle	5	0	100%	0.050
(d)	Independent	MPLE	0	0	0%	0.133
		LASSO	3.37	0	23%	0.112
		ALASSO	4.75	0.01	79%	0.064
		SCAD	4.92	0	92%	0.052
		MCP	4.92	0	92%	0.056
		Oracle	5	0	100%	0.044

### D.1.2 Highly Stratified

Table 10: Selection results of the penalized stratified model based on 100 replications with different censoring patterns, where  $\alpha_1 = 0.7$ ,  $K = 100$ ,  $n_k \in \{2, 3, 4, 5\}$ . The censoring rate is 27% and the event rate is 46%.

Scenario	Depend on	Penalty	C (5)	IC (0)	Pcorr	MMSE
(a)	$z_1, z_4$	MPLE	0	0	0%	0.168
		LASSO	3.60	0.01	20%	0.200
		ALASSO	4.82	0.04	81%	0.113
		SCAD	4.92	0.09	85%	0.070
		MCP	4.91	0.09	86%	0.070
		Oracle	5	0	100%	0.066
(b)	$z_5, z_8$	MPLE	0	0	0%	0.167
		LASSO	3.73	0.01	26%	0.199
		ALASSO	4.76	0.04	77%	0.124
		SCAD	4.88	0.11	83%	0.070
		MCP	4.88	0.13	83%	0.070
		Oracle	5	0	100%	0.063
(c)	$z_1, z_3$	MPLE	0	0	0%	0.174
		LASSO	3.59	0.01	29%	0.185
		ALASSO	4.73	0.06	75%	0.112
		SCAD	4.92	0.10	86%	0.069
		MCP	4.93	0.10	85%	0.069
		Oracle	5	0	100%	0.065
(d)	Independent	MPLE	0	0	0%	0.164
		LASSO	3.61	0	22%	0.178
		ALASSO	4.76	0.02	79%	0.097
		SCAD	4.90	0.06	88%	0.060
		MCP	4.90	0.05	87%	0.060
		Oracle	5	0	100%	0.058

## D.2 Penalized Marginal PSH Model

Table 11: Selection results of the penalized marginal model based on 100 replications with different censoring patterns, where  $\alpha_1 = 0.7$ ,  $K = 100$ ,  $n_k \in \{2, 3, 4, 5\}$ . The censoring rate is 29% and the event rate is 43%.

Scenario	Depend on	Penalty	C (5)	IC (0)	Pcorr	MMSE
(a)	$z_1, z_4$	MPLE	0	0	0%	0.101
		LASSO	3.36	0	15%	0.065
		ALASSO	4.77	0	83%	0.039
		SCAD	4.82	0	86%	0.034
		MCP	4.81	0	86%	0.033
		Oracle	5	0	100%	0.031
(b)	$z_5, z_8$	MPLE	0	0	0%	0.108
		LASSO	3.64	0	29%	0.067
		ALASSO	4.75	0	82%	0.033
		SCAD	4.80	0	86%	0.032
		MCP	4.83	0	87%	0.033
		Oracle	5	0	100%	0.031
(c)	$z_1, z_3$	MPLE	0	0	0%	0.104
		LASSO	3.58	0	22%	0.071
		ALASSO	4.80	0	84%	0.038
		SCAD	4.83	0	88%	0.034
		MCP	4.84	0	88%	0.034
		Oracle	5	0	100%	0.032
(d)	Independent	MPLE	0	0	0%	0.097
		LASSO	3.56	0	22%	0.060
		ALASSO	4.84	0	85%	0.035
		SCAD	4.88	0	91%	0.031
		MCP	4.84	0	85%	0.032
		Oracle	5	0	100%	0.029